Melodisplastik sindrom bilan og‘rigan bemorlarda kimyoterapiyaning infeksion asoratlari

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Annotatsiya: Miyelodisplastik sindromlar (MDS) - bu miyeloid naslning gematopoezidagi anomaliyalar bilan tavsiflangan kasalliklar guruhidir. Ushbu anomaliyalar natijasida yetuk qon hujayralarini ishlab chiqarish qobiliyati qisman saqlanib qoladi, lekin ba’zi turlari yetilmaydi va hujayralarning o‘zi o‘zgaradi. MDS bilan og‘rigan bemorlarning sezilarli qismi bir muncha vaqt o‘tgach, odatda bir necha oydan bir necha yilgacha o‘tkir miyeloid leykemiyani rivojlantiradi. MDS ba’zan “preleykemiya” deb ham ataladi va ilgari “past darajadagi leykemiya”, yoki “harakatsiz leykemiya” atamalari ham ishlatilgan. Bu suyak iligidagi blast hujayralarining tarkibi bilan bog‘liq: agar 20% dan ortiq (Jahon sog‘liqni saqlash tashkiloti tasnifiga ko‘ra) yoki 30% dan ortiq (Fransiya-Amerika-Britaniya FAB tasnifiga ko‘ra) bo‘lsa, biz miyeloid leykemiya haqida gapiramiz, ammo agar ularning darajasi chegaradan past bo‘lsa, MDS tashxisi qo‘yilishi mumkin.

Kalit so‘zlar: miyelodisplastik sindromlar, o‘tkir miyeloblastik leykemiya, kimyoterapiya,infeksion asoratlar, monoterapiya.

Infectious complications of chemotherapy in patients with melodysplastic syndrome

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Abstract: Melodysplastic syndromes (MDS) are a group of diseases characterized by abnormalities in hematopoiesis of the meloid lineage. As a result of these abnormalities, the ability to produce mature blood cells is partially preserved, but some types do not mature, and the cells themselves are altered. A significant proportion of patients with MDS develop acute meloid leukemia after some time, usually months to years. MDS is sometimes called “preleukemia” and has previously been referred to as “low-grade leukemia” or “dormant leukemia”. This is related to

the composition of blast cells in the bone marrow: if there are more than 20% (according to the World Health Organization classification) or more than 30% (according to the French-American-British FAB classification), we are talking about meloid leukemia, but if their level is below the threshold, a diagnosis of MDS can be made.

Keywords: melodysplastic syndromes, acute meloblastic leukemia, chemotherapy, infectious complications, monotherapy

MDS davolash simptomlarni yaxshilash va qo‘llab-quvvatlovchi yordam, shuningdek kimyoterapiya, ildiz hujayra transplantatsiyasi bilan o‘tkaziladi.

Odatda, davolash og‘ir alomatlari bo‘lgan bemorlar uchun ajratiladi.

Bemorlarga odatda doimiy qon va trombotsitlarni quyishni talab qilinadi. Bunday bemorlarda ko‘pincha temirning ikkilamchi ortiqcha yuklanishi, yani gemosideroz rivojlanadi. Bunday hollarda temir xelyatsiyasi, yani xellatoterapiya o‘tkaziladi va bu past xavfli miyelodisplastik sindromi va ferritin darajasi >1000 ng/ml (>1000 mkg/L) bo‘lgan bemorlar uchun foydali bo‘lishi mumkin.

Eritropoezni stimullovchi vositalar (ESV) MDS bilan og‘rigan bemorlarning 15-20 foizida anemiyani kamaytiradi, ayniqsa qon zardobida eritropoetin darajasi <500 mIU/ml (<500 IU/L) bo‘lgan bemorlarda. Halqali sideroblastlari bo‘lgan refrakter anemiyada eritropoezni stimulyatsiya qiluvchi vositalar (ESV) va granulotsitlar koloniyasini stimulyatsiya qiluvchi omil (G-CSO) bilan davolash eritroid hujayralarining javob tezligini taxminan 40% ga oshirishi mumkin. Biroq, MDSning barcha shakllarida o‘sish omillari (ESv + G-CSF) bilan davolash bemorni axvolini yaxshilamaydi va/yoki O‘MLga o‘tish xavfini kamaytirmaydi. ESV terapiyasi muvaffaqiyatsizlikka uchragan halqali sideroblastlari bo‘lgan juda past xavfli o‘rta xavfli MDSga ega bemorlarda gematokritni muvaffaqiyatli oshirdi.

Miyelodisplastik sindromni davolash uchun ishlatiladigan kimyoviy dorilar:

Azatsitidin, Detsitabin, Lenalidomid.

Azatsitidin - pirimidin nukleozid analogidir. Azatsitidin qo‘llab-quvvatlovchi davolash va an’anaviy kimyoterapiya bilan solishtirganda umumiy omon qolishni uzaytiradi. Azatsitidin bilan davolangan barcha MDS subtiplari bo‘lgan bemorlarning o‘rtacha omon qolish muddati 21 oyni tashkil qiladi. Davolanish kamida 4-6 sikl davomida o‘tkazilishi va bemorning foyda olishda davom etishi kerak.

Desitabin ham pirimidin nukleozid analogidir. MDS bilan kasallangan bemorlarning 43% gacha remissiyaga olib keladi. Ushbu preparat barcha MDS subtiplari bo‘lgan bemorlarni davolash uchun ko‘rsatiladi.

Azatsitidin va detsitabin DNKni gipometilatsiya qiluvchi epigenetik modulyatorlardir. Ba’zi DNK mintaqalarining metilatsiyasining kuchayishi o‘simta bloklovchi genlarga zarar yetkazadi va MDSda onkogenezda muhim rol o‘ynaydi.

Lenalidomid - MDS sindromi bo‘lgan bemorlarda qizil qon tanachalarini quyish zaruratini kamaytirishda samarali bo‘lgan immunomodulyatordir.

Gipoplastik MDS bilan og‘rigan bemorlarda antitimotsit globulin (ATG) bilan yoki siklosporin bilan immunosupressiya samarali ekanligi isbotlangan, bu hujayralar sonining ko‘payishi va qon quyish ehtiyojining kamayishi bilan tasdiqlanadi.

Allogenik gematopoetik ildiz hujayralarini transplantatsiya qilish miyelodisplastik sindromni davolashning yagona usuli hisoblanadi. Allogenik gematopoetik ildiz hujayralari transplantatsiyasi tibbiy kontrendikatsiyaga ega bo‘lmagan yosh bemorlarga, odatda o‘rta 2 va yuqori xavfli guruhlarga ko‘rsatiladi. Kimyoterapiya (KT) paytida yuqori xavfli MDS va ML MD bo‘lgan bemorlarda infeksiyalar keng tarqalgan asoratlardir .

Maqsad: Kimyoterapiyaning birinchi kursida (KT) yuqori xavfli MDS va ML MD bilan og‘rigan bemorlarda yuqumli asoratlarning chastotasi va tabiatini solishtirish.

Materiallar va usullar: Tadqiqot 2022 yildan 2024 yilgacha Samarqand viloyat ko‘p tarmoqli tibbiyot markazi gematologiya markazida o‘tkazildi va yuqori xavfli MDS va MLMD tashxisi qo‘yilgan 16 bemorlarni o‘z ichiga oldi. Monoterapiya kurslaridan so‘ng yuqumli asoratlar tahlil qilindi. gipometillovchi dorilar (GMD) Azatsitidin (Aza) (n=40) yoki Detsitabin (Dets) (n=17) va gipometillovchi dorilar bilan past dozali kimyoterapiya tayyorlash Aza - Ida - Ara -C (n=21) yoki Dets - Ida - Ara -C (n=10). OMF monoterapiyasini olgan bemorlar guruhidagi yuqumli asoratlarning chastotasi va tuzilishi taqqoslangan (p =0,145), bu ularni bir guruhga birlashtirishga imkon berdi. Xuddi shunday holat Aza - Ida - Ara -C va Dets - Ida - Ara - kursini olgan bemorlar guruhlarida kuzatildi (p=1.000). Shunday qilib, keyingi tahlillar OMF monoterapiyasi va kombinatsiyalangan kimyoterapiyani olgan bemorlar guruhlarini taqqoslashga asoslangan .

Natijalar: Tadqiqotda 28 yoshdan 67 yoshgacha bo‘lgan (o‘rtacha 55 yosh) 16 bemor (9 erkak,7ayol)ishtirok etdi. OMF monoterapiyasi 9 (70%) bemorga, kombinatsiyalangan terapiya 5 (35%) bemorga o‘tkazildi. Monoterapiyaning birinchi kursida bemorlarning aksariyati 56 yoshdan oshgan (61%, n=23ga qarshi 16%, n=3, p <0.001), yuqori xavfli MDS tashxisi (84%, n=32ga qarshi 26%, n=8, p<0.001, gipotsellulyar 18%). n=5, p=0,012), trombotsitlar soni <40×10x9/l (29%, n=11 ga qarshi 3%, n=1, p=0,005), leykotsitlar soni <3.5×109/l(74%, n=28 ga qarshi 52%, n=16, p =0.). Kimyoterapiyaning birinchi kursi davomida infeksiyalar OMP monoterapiyasidagi bemorlarning 65% (n=38) va kombinatsiyalangan kimyoterapiyadagi bemorlarning 100% (n=31) da (p<0,001) kuzatilgan. Agranulotsitozning rivojlanishi (leykotsitlar <1×109/l) monoterapiya va kombinatsiya kurslaridagi bemorlarning 37% (n=16) va 87% (n=19) da birinchi kimyoterapiya kursini murakkablashtirdi (p<0,001). Ikkala guruhda ham klinik

jihatdan tasdiqlangan infeksiyalar ustunlik qildi (79%, n=30 va 74%, n=23), so‘ngra nomalum etiologiyali isitma (17%, n=3 va 16%, n=4), qon oqimi infeksiyalari (6%, n=2 va 16%, n=4). Infeksiyalar orasida yetakchi o‘rinni pnevmoniya (70%, n=21 va 74%, n=17) egallagan bo‘lsa, kombinatsiyalangan kimyoterapiya kursida bo‘lgan bemorlarda 41% hollarda pnevmoniya o‘tkir nafas etishmovchiligi rivojlanishi bilan birga kelgan. Pneumotsistik pnevmoniyasi 5 % (n=1) va 12% (n=2) hollarda, lungellyoz mos ravishda 5% (n=1) va 6% (n=1) da tashxisqo‘yilgan. OMP monoterapiya kursida MDS bo‘lgan 2 (5%) bemorlarda invaziv aspergillyoz aniqlandi. Gerpes virusli infeksiyalarning chastotasi taqqoslangan va mos ravishda 26% (n = 7) va 32% (n = 7) ni tashkil etdi. 14 ta holatdan 12 tasida (86%) virusli infeksiya Gerpes tomonidan qo‘zg‘atilgan simpleks, 2 (14%) da - gerpes virusi turi bilan monoterapiya rejimida OMP kurslarini olgan bemorlardan farqli o‘laroq, 42% (n=12) hollarda kombinatsiyalangan kimyoterapiya kurslaridan so‘ng bir nechta yuqumli asoratlar qayd etildi 12% (n=5) (p=0,006).

Xulosa: Monoterapiya rejimida OMP terapiyasini o‘tkazish samarali davolash usuli bo‘lib, kamroq yuqumli asoratlar bilan birga keladi. OMP monoterapiyasidan keyin agranulotsitozning rivojlanishi va yuqumli asoratlarning chastotasi gipometilizatsiya bilan past dozali kimyoterapiya kurslariga nisbatan sezilarli darajada past edi. Shu bilan birga, yuqumli asoratlarning xilma-xilligi diqqatga sazovordir: bakterial infeksiyalarga qo‘shimcha ravishda, invaziv o‘pka aspergillyozi, Pnevmotsistik pnevmoniyasi va gerpesvirus infeksiyalari tashxisi qo‘yilgan.

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