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Artesunate Resistance in Plasma Diumfalciparum Malaria

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Abstract: *The World Health Organization has urged to set up art emisin in based combination herapy (artemisininandeffectiveantimalarialdrug)andgraduallypulloutoralartemisininmono-therapiesfromthemakingofprescriptionduetotheirhighrecrudescenceratesandtoreducetheriskofdrugresistance.We presentararecasefromSouthGujaratregion,admittedinNCH,SuratwithArtesunateresistantPlasmodiumFalciparum malaria.InIndianliteratureandclinicalpractiseararecaseisreportedhere.*

Keywords: *Malaria;Plasmodiumfalciparum;Artesunate; ACT;DrugResistant.*

I. Introduction

Artemisininresistanceisdefinedasdelayedparasiteclearancefollowingtreatmentwithanartesunatemonotherapy,oraftertreatmentwithanartemisinin-basedcombinationtherapy(ACT).TheWorldHealthOrganization(WHO)recommendstheuseofartemisininderivativesonlyincombinationwithefficientpartnerdrugsagainstPlasmodiumfalciparummalariatomakesurehighcureratesandpostponementresistance.

Artemisininsproducerapidtherapeuticresponse,reducegametocytecarriage,andarewelltoleratedbypatients[1].ThefiveformulationsofArtimisininCombinationTherapy(ACT)areartemether +lumefantrine,artesunate+mefloquine,artesunate+amodiaquine,artesunate+sulphadoxine-pyrimethamine,anddihydroartemisinin+piperaquine[2].TheACTwasintroducedbytheNationalVectorBorneDisease ControlProgramme(NVBDCP)asthefirst-linetreatmentoffalciparummalaria.PresentlyallformulationsofACTrecommendedbyWHO,exceptDihydroartemisinin+piperaquine,areregisteredwiththeDrugControllerGeneralofIndiatotreatthepatientaswellastoovercometheresistantpropertyofP.falciparum.

II.Casereport

ThisreportstatedaninvivoartesunateresistantPlasmodiumfalciparumcaseinSurat,Gujarat.Amalepatient,65 yearsofage,wasaresidentofSouthGujarat,Surat,India.Thepatientwassufferingfromfeverwithchillandrigoronalternatedaysforthepastfourdays.Patientwasadmittedforthesamein NewCivilHospital,Suraton24.10.15.Boththick(Giemsastained)andthin(Leishmanstained)filmsofthepatientwereobserved in theperipheralblood smear, in NCH,Pathology Laboratory.Microscopic observationsuggested thepresence of P. falciparum ringsand trophozoitesin his bloodand P.falciparumantigenwasalsodetectedwithmalariaparasiteindex4.9.HewasstartedonArtesunateinjection120mgi.v.andgivenSulfadoxinepyrimethamineonthefirstdayofhisadmission(24.10.15)followedby120mgi.v.12hourly.Thiswasfollowedby120mgi.v.onceadayfornextfourdays.But,evenafter5daysofArtesunatehisbloodperipheralsmearshowedringsandtrophozoitesofplasmodiumfalciparummalariaewithmalariaparasiteindexof4.6.andP.falciparumantigenwasalsodetected.Thetreatmentwascontinuedfor7days.On30.10.15hismalariaparasiteindexwas4.5withringsandtrophozoites.Thistimehewastreatedwithsixtabletsofartemether80mgandlumefantrine480mg(LumetherforteDT)from1.11.15 administeredorallyat0,6,24,36,48and60hr.Hebecameafebrilefrom3.11.2015.HisbloodshowedgametocytesofP.falciparum.Hehadnohistoryofmovement to neighboring countriesin recent years. Theseresults demonstratedthatthe patientwasclinicallyresistanttoartesunate.Itwasatreatmentfailurecase.However,thecombinedtherapy(artemetherand lumefantrine)waseffectiveinhiscase.

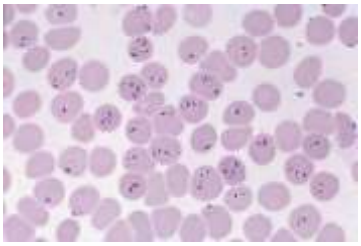

Fig 1:Artesunateresistantrings of Pfalciparum

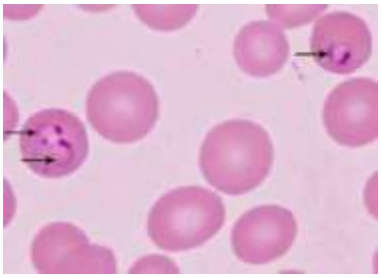

Fig 2:Artesunateresistanttrophozoitesof Pfalciparum

III. Discussion

ThepresentnationaldrugpolicyisACT(artemisininandSP)[5].In2007,artesunateplussulfadoxine–pyrimethaminewasselectedasthefirstlinetreatmentinhighriskdistrictsandareaswithidentifiedresistance,withthegoalofcoveringmostoftheŶatioŶ'sPfalciparumburden.In2010thistreatmentbecamethefirstlinetreatmentthroughoutIndia[5].Indiahasthelargestpopulationintheworldatriskofmalaria,with85%livinginmalariouszones[6].Artemisininď'asedĐoŵďiŶatioŶtherapy;ACT□isthefirstlinetreatmentoffalciparummalariarecommendedbytheWorldHealthOrganization[1].Theartemisininderivativesproviderapidandeffectivereductionofparasitebiomassandgametocytecarriage[7,8],whilethepartnerdrugsinACTsareeliminatedmuchmoreslowly,providingmutualaugmentationofeffiĐaĐyaŶdproteĐtioŶfroŵresistance[9,10,11].WidespreaddeploymentofACTsisoneofthemainfactorsunderlyingrecentreductionsinglobalmalariamorbidityandmortality[12,13,14].Unfortunately,reducedinvivosusceptibilitytoartemisininderivatives,manifestbyprolongationofparasiteclearancetimes,hasemergedinCambodia[15,16,17,18]and,morerecently,onthenorthwesternborderofThailand[19].ACTeffiĐaĐyiŶtheseareasisfalliŶg[20].

EmergenceofresistancetoACTwasfirstreportedin2009byDondorpetal.,showingdelayedparasiteClearanceratesinPailin,WesternCambodia.Resistanceisnowviewedasthesequelaeofwidespreaduseofthisdrugandtheratesofspreadareaccentuatedbythesocioeconomicconditionsindifferentgeographicregions[21].Indiasharescommonborderwiththeseregionsandthethicklandscapemightfavorvectortransmissionandenablespreadofresistancetoindia.Delayedparasiteclearancewillnotnecessarilyleadtotreatmentfailure.IntheGreaterMekongsubregion(GMS),ahightreatmentfailureratefollowingtreatmentwithanACThasonlybeenobservedwherethereisresistancetothepartnerdrug,regardlessofthepresenceofartemisininresistance.However,artemisininresistancecouldfacilitatetheselectionofpartnerdrugresistance.MutationsintheKelch13(K13)propellerregionareassociatedwithdelayedparasite clearanceboth in vitroand in vivo.TheidentificationoftheK13markerforartemisininresistancehasallowedforamorerefineddefinitionofresistance[22].Inviewoftheabovefindingstogetaclearpictureofartemisininresistanceof*P.Falciparum,*athoroughstudyisrequiredinvolving*invivo*,*invitro*andmolecularprocedures.Thiscasesuggeststhatcombinationtherapyeffectiveaswellasartesunateandlumefantrineinsuchcasesismorepracticableandefficaciousthananyothercombination.

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