Casestudy

Epithelioidhemangioendotheliomaoftheliver:acasereport

Abstract

Epithelioid Hemangioendothelioma of the liver (EHE) is a rare primary solidtumor of vascular origin. It develops in a non-cirrhotic liver and its pathogenesisremainsunknown.Theinvolvementisoftenmultinodularandmaymimicmetastases of a primary extrahepatic lesion and may delay the diagnosis. Theclinicalandbiologicalsignsarenon-specific.Anatomopathologicaldiagnosiscanbe difficult, requiring the precious help of immunohistochemistry. We report theclinical case of a 22-year-old patient admitted with febrile right hypochondrialpain,peritonealandpleuraleffusionsyndromewithaseverealterationofgeneralcondition. The diagnosis of hepatic EHE was proven on immunohistochemicalstudyoftheliverbiopsy.Theevolutionwasmarkedbythedeath ofthepatient.

Keywords:Liver;Haemangioendothelioma

Comment [D1]: If possible, mention about incidence rate. How rare or how common this entity is?

Comment [D2]: You can add more relevant keywords

INTRODUCTION

Epithelioid hemangioendothelioma of the liver (EHE) is a rare vascular tumorwithintermediatemalignantpotential,firstdescribedattheexpenseofsofttissuein 1982 by Weiss et al [3,10]. It can involve several organs, including the liver,lung and bone.Hepatic localization is exceptional and usually multifocal, whichmay radiologically simulate secondary localizations [6, 9]. We report the clinicalcase of a 22-year-old patient with an epithelioid hemangioendothelioma of theliversimulatingsecondarylesionsandprovenbyimmunohistochemicalstudy.

casepresentation

A22-year-oldpatient,chronicuserofhookahweaned6monthsago,washospitalizedforfebrilepainoftherighthypochondrium.Thehistoryofthediseasewentbacktosevenmonths,withtheprogressiveinstallationofapainoftherighthypochondrium associated with afever quantifiedat 38-39° degree withouticterus, the whole evolving in a context of alteration of the general state made ofasthenia,anorexiaanduncalculatedweightloss.Theclinicalexaminationshowedapainfulhardhepatomegalywithahepaticarrowat18cmandasciteswithoutanysignofportalhypertensionorhepatocellularinsufficiency.Biologically,thebloodcount showed a normocytic normochromic regenerative anemia at 8 g/dl withhyperleukocytosisat12470elements/mm3,acorrectplateletcountwithahighC-reactiveproteinat227mg/l.Thehepaticwork-upshowedabiologicalcholestasiswith gamma-GT at 178IU/L, alkaline phosphatases at 292IU/L with a slightelevationoftotalbilirubinat13.6mg/lwithapredominanceofconjugatedat8.1mg/landminimalcytolysisonASTat58IU/landnormalALTat23IU/l.albumin was low at 26g/l with prothrombin and factor V at 80% and 119% respectively.Abdominalultrasoundshowedanenlargedliver,withregularcontours, heterogeneous,associatedwithmultiplenodularlesionsandaperitonealeffusionlayer .Thethoracoabdomino-pelvicCTscanwithcontrastinjectionshowedmultiple bilateral diffuse pulmonary nodules of random arrangement, the largestat the right apical level of 10×8mm and left basal level of 9×8mm, with a smallright pleural effusion (**Figure 1, 2**). At the abdomino-pelvic level, the liver wasincreased in size by 20 cm, with bumpy contours, heterogeneous, with multiplenodularandpatchylesions,hypodense,confluent,notenhancedafterinjectionofthecontrast,themostvoluminousoneisunder capsulardefectstraddlingsegments V, VI and VII measuring 180 mm anteroposteriorly, 103 mm in widthand171mminheight,associatedwithamedium-sizedperitonealeffusionwithoutdeepabdominaladenopathiesorsuspicious-lookingbonelesions(**Figure**

Comment [D3]: Use better term instead of “installation”

Comment [D4]: Grammar correction

3, 4). All this suggests secondary pulmonary, hepatic and peritoneal localizations.Theetiologicalinvestigationwasnegativeinsearchofaprimarytumor,bymeansof fibroscopy and colonoscopy. Tumor markers (CEA, CA19-9 and alpha-feto-protein) were negative. An echo-guided liver biopsy was performed, revealing atumor-likenecrosiswithsomeatypicalcellsandimmunohistochemicalexpressionofCD31andCD34,withoutexpressionofHHV8infavorofahepaticepithelioid hemangioendothelioma. The evolution was marked by the worseningof the clinical picture with the appearance of jaundice, bilateral pleurisy and thebiological picture with gamma-GT at 214IU/l, PAL at 365IU/l, total bilirubin at76.4mg/lwithapredominanceofconjugatedbilirubinat59.7mg/l,acutecytolysiswith a level of ASAT at 642IU/l, ALAT at 99IU/l and a PT at 40%. The patientdiedbefore recoveryofthe resultfrom theIHC study.

Comment [D5]: Mention about figure 5 here

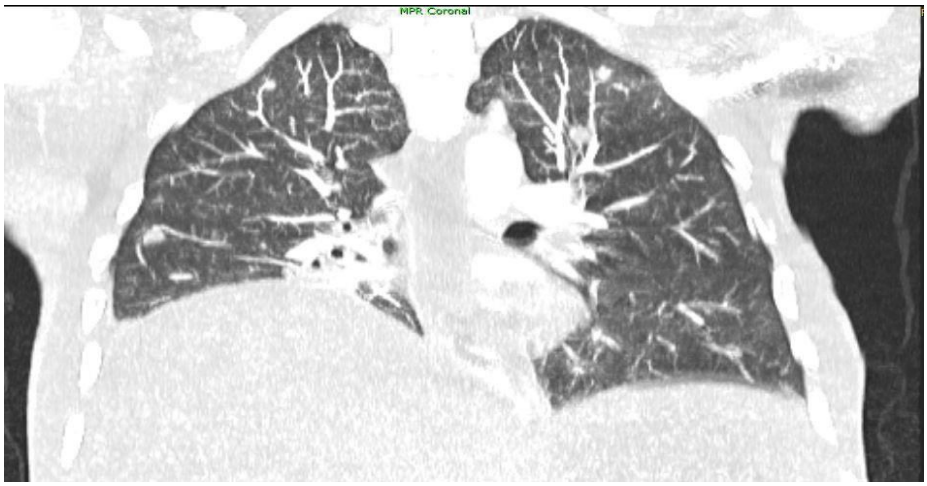
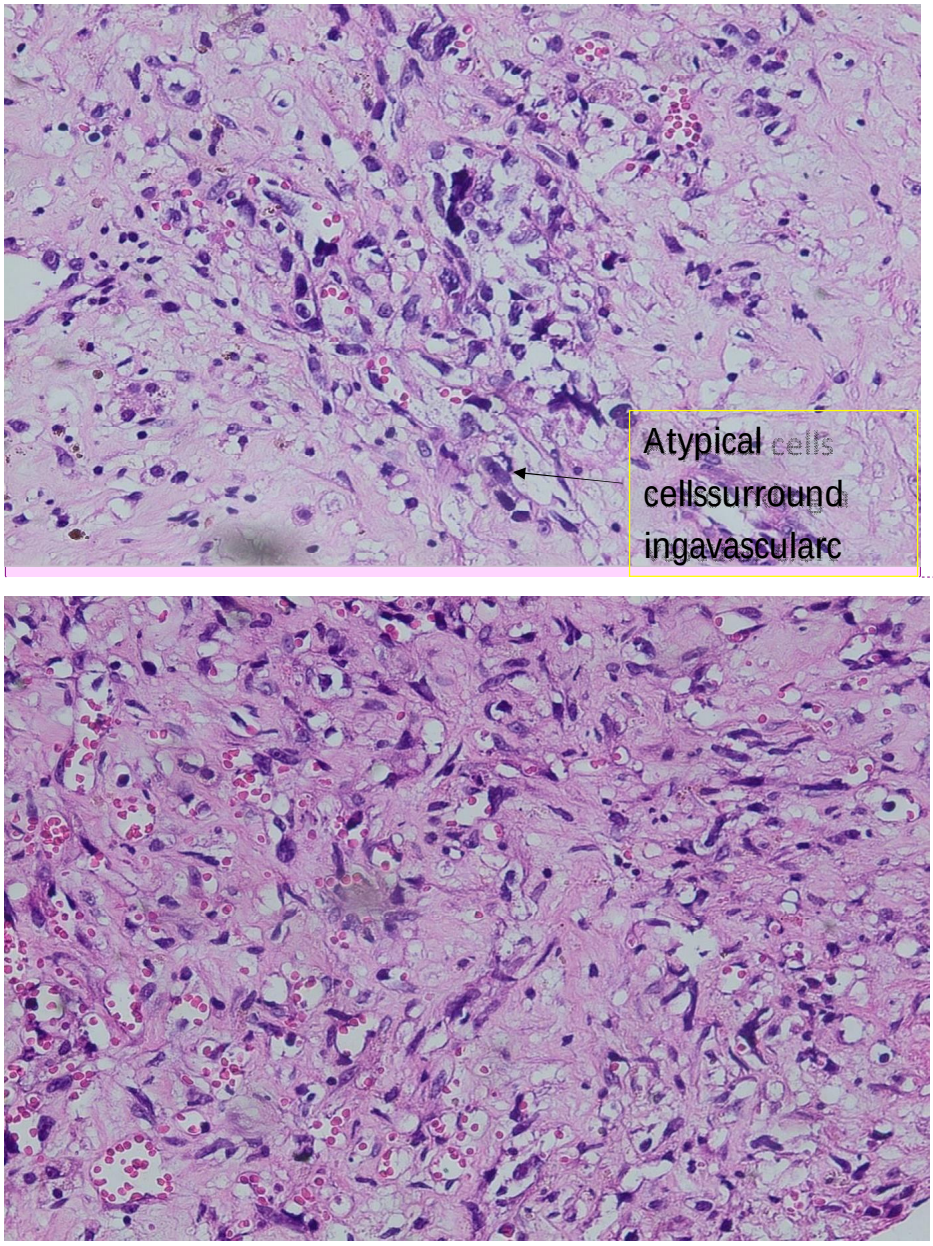


Figure1ChestCTlongitudinalsectionwithinjectionofmultiplebilateraldiffusepulmonarynodules,right apicalandleftbasal,with asmallright pleuraleffusion

Figure2:ChestCTaxialsectionwithinjectionofmultiplebilateraldiffusepulmonarynodules,rightapical andleftbasal, witha smallright pleuraleffusion

Figure3:Axialsection abdominalCTtheliver wasincreasedinsizewithbumpycontours,heterogeneous, seat of multiple lesions nodular and patches, hypodense, confluent non-enhancedafterinjection of PDC

Figure4: Axialsection abdomino-pelvicCTrisingperitonealeffusion



Comment [D6]: Label individual microscopic image, including which stain, what power is focused under microscope

fig.5Liverbiopsy:itisafibrousfragmentwithvascularslitsborderedbyatypicalcellswithadense,irregularnucleusandaneosinophiliccytoplasmthatissometimesvacuolated.

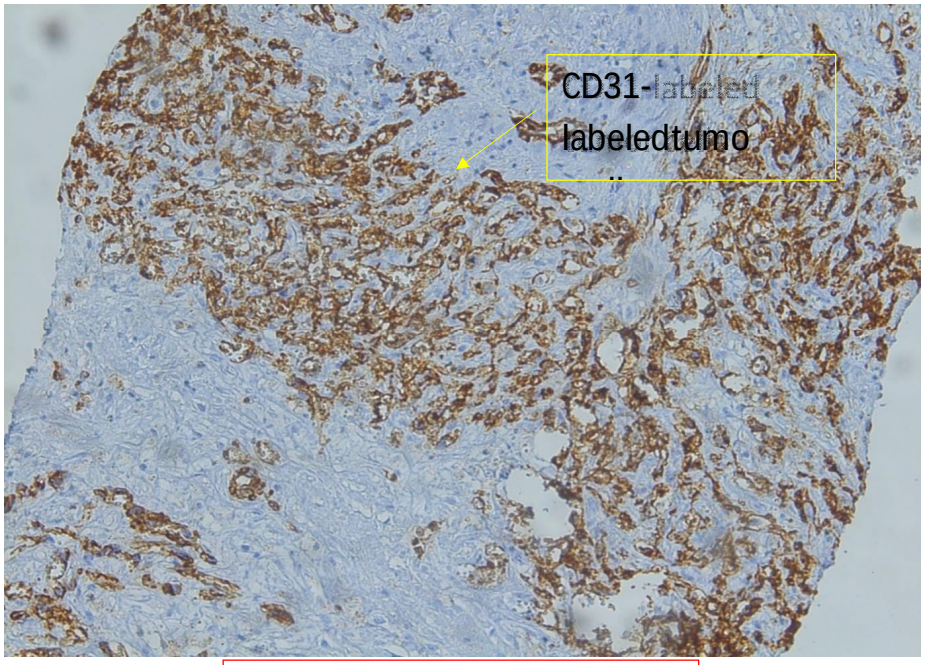


fig.6ThetumorcellsexpressCD31.

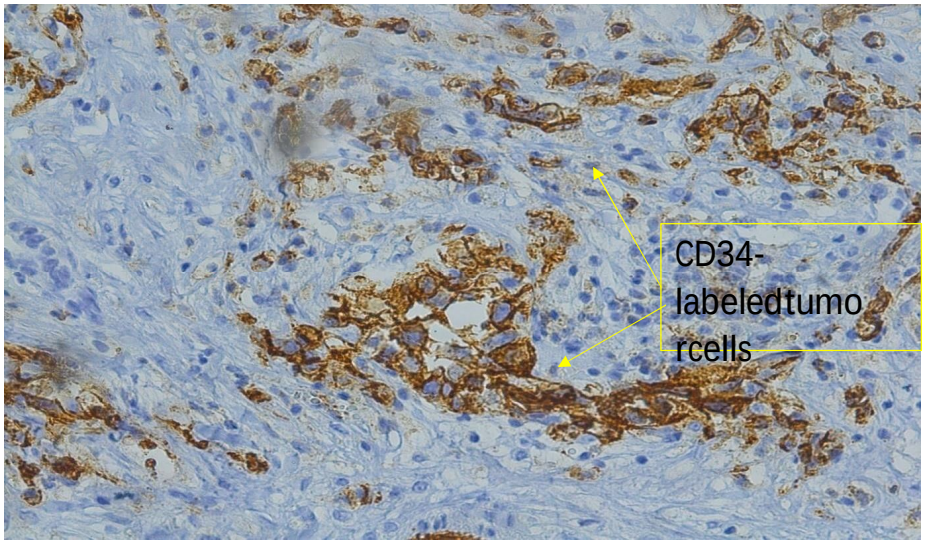


fig.7ThetumorcellsexpressCD34.

DISCUSSION

Epithelioid hemangioendothelioma is a rare solid tumor, vascular in nature, ofuncertain evolution, with intermediate malignancy between benign hemangiomaand angiosarcoma, first described in 1982 by Weiss et al [1, 3, 10]. It usuallydevelopsinsofttissueorbone.Thisdiseaseusuallyaffectssubjectsintheirfourthdecadewithaslightfemalepredominance[4,12].PrimaryhepaticlocalizationofEHE is exceptional and approximately 50% of cases are initially metastatic, withpulmonary or bone involvement at the time of diagnosis [5, 7]. No etiologicalfactors have been identified, and there is no evidence ofcontraceptive role[1,8,10, 12]. The clinical symptomatology of liver EHE is non specific. In themajority of cases, it may present with right hypochondrial pain, altered generalcondition, and fever as in our clinical case. The discovery can also be fortuitousduringanabdominalultrasound.Andexceptionally,itcanberevealedbyaBuddChiari syndrome following invasion of the suprahepatic veins, hemoperitoneumby intraperitoneal rupture, hepatocellular insufficiency or portal hypertension [5,9].

Comment [D7]: Grammar correcion

Biologically,thereisnospecificmarkerandliverbalancedisturbancesareinconsistentatthetimeofdiagnosis.Moderateelevationofalkalinephosphatasesis observed in 75% of cases, gamma-glutamyl transferases in 16% of cases andtransaminases in 10% of cases [2, 6, 10, 11]. Tumor markers (alpha-fetoprotein,CEAandCA19-9)werenegative.Theradiologicalappearanceisnotunambiguous; in the early phase, it is often multinodular with a halo appearance.These lesions will coalesce to form diffuse, infiltrative lesions that may mimicmetastases of a primary extrahepatic lesion and may delay diagnosis [6]. On CTscan, nodular lesions are hypodense on non-injected time with halo contrast oninjected time and become isodense on portal time [6]. On magnetic resonanceimaging,thelesionsarehypersignalonT2sequencewithanecroticcenter,often

hyposignal after gadolinium injection [2, 6, 9]. Our patient had a CT appearancein favorofsecondaryhepatic,pulmonary andperitoneal lesions.

Extrahepaticlocalizationsarecommonandpresentin30%ofcasesatthetimeofdiagnosis,andourpatienthadperitonealandpulmonarymetastasesatthetimeofdiagnosis [14].

Thehistologicaldiagnosisisdifficultandoftenerroneousbecauseofthehistological similarities with hemangioma and angiosarcoma. For this reason,immunohistochemical study is essential to confirm the diagnosis by showing thepositivityofendothelialcellmarkerssuchasfactorVIII,CD31andCD34[6,13].

TheevolutionofEHEisunpredictable,rangingfromtheslow-growingformwithnoimpactonthegeneralstatetothedarkerformrapidlyprogressingtohepatocellularfailure.Managementisadaptedtoeachindividualcaseandisbasedon radiological surveillance, surgical removal of lesions, chemotherapy or livertransplantation [2, 10, 14]. The overall five-year survival of patients with EHE isestimated tobe28-30%dependingon the series[4,8].

Conclusion

Epithelioid hemangioendothelioma of the liver is an orphan disease. Primaryhepaticlocalizationisrare.Itsdiagnosisremainsdifficult,requiringtheuseofanimmunohistochemical study. The prognosis is variable and may be poor in somecases.Thetherapeuticmanagementisadaptedaccordingtothepresentationofthe hepatic involvement, the symptomatology of the patient and the rapidity of theevolution.

Références:

1- S. Ouakri, M. Boutajanouit, K. Ahchari, A. Hamri, Y. Narjis and R. Benelkhaiat. EPITHELIOIDHEMANGIO-ENDOTHELIOMAOFTHELIVER:ABOUTARARECASE:Int.J.Adv.Res.2022;10(03)877-881

2- A Askri, S Mannai, S Landolsi, L Ben Farhat, W Said, N Dali, MT Khalfallah and L Hendaoui.Hepaticepithelioidhemangioendothelioma:about 3cases.J.Radiol2009;90:310-4

3- S.Azzabi,W.BenGhezala,I.Boukhris,A.Hariz,I.Kéchaou,E.Chérif,C.Kooli,Z.Kaouech,L.Ben Hassine, N. Khalfallah. Epithelioid hemangioendothelioma of the liver: a new case. TheJournalofInternalMedicine35S(2014)A86-A200

4- F. Demuynk, J. Morvan, C. Brochart et al. Epithelioid hemangioendothelioma of the liver: arare livertumor. JRadiol2009,90:845-8

5- Abderrahmen Ammar, Mahdi Abbdennadher, Hazem Zribi, SarraZairi, Ahmed Ben Ayed,AidaAyadiKaddour,SoniaOuerghi,AdelMarghli.Pulmonaryepithelioidhemangioendothelioma: an entity to be evoked in the differential diagnosis of pulmonarymetastases.Journal.sfctcv.org 2017;5:T-34

6- W. BizimanaA.HouchiIckambaW. AmarkakH.JerguigueR. LatibY.Omor.Hepaticepithelioidhemangioendothelioma:thelollipopsign.NationalInstituteofOncology,Mohamed V University, Rabat, Morocco. Journal of diagnostic and interventional imaging2020;xx:1-2

7- Sophie Cousin, François Le Loarer, Amandine Crombé, Marie Karanian, Véronique Minard-Colin,NicolasPenel.Epithelioid hemangioendothelioma.BullCancer2019; 106:73-83

8- F. Maisonnette, S. Hardemann, T. Abita, S. Durand-Fontanier, D. Valleix, B. Descottes.Epithelioidhemangioendotheliomaoftheliver:aboutaclinicalcaseandreviewofthelite rature.Annalesdechirurgie131(2006)115-117

9- J. Schmidt, L. Dessort, D. Chatelainb, R. Cévallosa, P. Duhauta, J.-P. Ducroixa. Epithelioidhemangioendothelioma of the liver: about a case. La Revue de médecine interne 28 (2007)S83-S160

10- F.Isfan,F.Deméocq(1),D.Dalnes(2),J.M.Garnier(1),J.Joubert.Hepaticepithelioidhemangioendothelioma(HEH).ArchivesdePédiatrie2010;17 :1-178

11- BahiZamouri. Epithelioid hemangioendothelioma. Descriptive study and case report. LifeSciences.2011.ffhal-01732302

12- GabrieleBarabino,AdinaPetcu,MurielCuilleron.Ararelivertumor,EpithelioidHemangioendothelioma.LaLettredel'Hépato-gastroentérologue.2016; Vol.XIX-N1

13- S. Fenniche, R. Benmously et al. Cutaneous epithelioid hemangioendothelioma. AnnDermatoVenereol.2004;131:818-21

14- O. Leleu et al. Pulmonary hemangioendothelioma: about three cases and review of theliterature.Revuedesmaladiespulmonaire,2010;27:778-783

Comment [D8]: Write as per Vancouver reference style

Comment [D9]: Write as per Vancouver reference style

Comment [D10]: Write as per Vancouver reference style

Comment [D11]: Write as per Vancouver reference style

Comment [D12]: Write as per Vancouver reference style

Comment [D13]: Write as per Vancouver reference style