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◇ CASE REPORT ◇

造影超音波検査の後血管相で不整形高エコー像を認めたPD-1抗体薬に起因する肝機能障害の1例

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抄　録

症例は60代，男性．左舌癌・頸部リンパ節転移に対し，切除術とリンパ節郭清が施行され，2ヵ月後に局所再発，骨転移のため化学療法施行されるもProgressive Diseaseと効果判定された．免疫チェックポイント阻害剤のニボルマブを使用し，3クール投与後，ASTとALT高値のGrade 4の肝機能障害（CTCAEv 4. 0）が出現した．発症日の造影MRIにて肝S 2に腫瘤を認めたが，その他の部位に血流異常は認めなかった．第8病日，ソナゾイド造影超音波検査で，後血管相において肝実質に不整形な高エコー像が不規則に分布していた．発症日よりプレドニゾロン，第8病日よりミコフェノール酸モフェチルの投与を開始しASTとALTの改善を認めたが，徐々にビリルビンの上昇を認めた．第10病日に超音波ガイド下肝生検を施行し，肝実質に一様にCD 3陽性細胞やCD 68陽性細胞の軽度増生を認めた．第42病日に造影超音波を再検したが，前回と変化なく，第43病日に超音波ガイド下肝生検を再検し，前病理所見に加えて胆汁うっ滞増悪所見を認めた．肝機能障害改善に合わせて免疫抑制剤の用量の漸減と中止を行ったが，サイトメガロウイルス肺炎を発症し，第66病日に死亡した．ソナゾイドによる造影超音波の後血管相において本症例のような不整形な高エコー像を呈す画像所見の報告は少なく，肝機能障害を合併したきわめて稀な症例を経験したため報告する．

A case of irregular high spots on contrast-enhanced ultrasound image of high level of AST and ALT due to anti-PD-1 antibody

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Abstract

A 61-year-old man underwent resection for tongue cancer and dissection for cervical lymph node metastases. Two months after the surgery, he experienced local recurrence of tongue cancer, which had spread to cervical and mediastinal lymph nodes and multiple bones. Liver dysfunction, i.e., a high level of AST and ALT（CTCAE Grade 4）, occurred 7 days after three courses of nivolumab, which had been administered owing to tumor progression that was noted despite first-line chemotherapy using docetaxel, cisplatin, and 5-FU. An abnormality of the blood flow was not observed by contrast-enhanced MRI. Oral prednisolone（PSL）（2 mg/kg/day）therapy was started immediately. Mycophenolate mofetil（1, 000 mg/body）was added to the PSL therapy 8 days after detection of the liver dysfunction. In a contrast-enhanced ultrasound imaging study using Sonazoid, irregular high spots were observed in the whole hepatic parenchyma in the post-vascular phase. Drug-induced liver injury was pathologically diagnosed by an ultrasound-guided needle biopsy 10 days after onset of liver dysfunction. Immunohistochemically, the number of CD3- and CD68-positive cells had slightly increased throughout the whole liver parenchyma. The levels of transaminase decreased, but the level of total bilirubin increased gradually. In a contrast-enhanced ultrasound imaging study using Sonazoid, the same image was observed in the whole hepatic parenchyma in the post-vascular phase 42 days after occurrence of liver dysfunction. The patient died of cytomegalovirus pneumonia and tumor progression 66 days after emergence of liver dysfunction. This is the first case report of irregular high spots in the post-vascular phase detected by contrast-enhanced ultrasound using Sonazoid in a case of nivolumab-induced liver dysfunction.

Keywords

nivolumab, Sonazoid, drug-induced liver dysfunction

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