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CASE REPORT

Fronto-parietal osteoblastoma with secondary aneurysmal bone cyst: A case report

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KEYWORDS
Osteoblastoma;
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Secondary;
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Summary *Background:* Osteoblastomas and aneurysmal bone cysts each comprise 1% of primary bone tumours. As both osteoblastomas and aneurysmal bone cysts are not common, osteoblastomas with secondary aneurysmal bone cysts of calvaria are extremely rare. Only three cases describing a secondary aneurysmal bone cyst in the setting of a calvarial osteoblastoma can be found in the literature. We report the case of the surgical resection of the fronto-parietal osteoblastoma accompanying a secondary aneurysmal bone cyst.

Case description: The case is a 24-year-old male with a 2-year history of a painless lump in the hair-bearing region of the left fronto-parietal area without neurologic symptoms. Computed tomography showed an intradiploic tumour with maintained inner and outer cortex of the left front-parietal bones. 3.0-T magnetic resonance imaging showed a well-circumscribed, intradiploic, multilocular cystic tumour.

A gadolinium-enhanced sequence showed strong peripheral and septal enhancement. These findings were consistent with an osteoblastoma associated with secondary aneurysmal bone cyst. An *en bloc* tumour resection with a 10-mm horizontal margin was completed without complications. The calvarial defect was covered by calvarial bone graft harvested from the contralateral fronto-parietal bone. The postoperative course was uneventful. Pathological diagnosis was consistent with the osteoblastoma with secondary aneurysmal bone cyst. After a follow-up period of 2 years, there was no evidence of recurrence.

Conclusion: The combination of osteoblastoma and aneurysmal bone cyst of the calvaria is a rare clinical entity. Careful preoperative examination and complete resection of the tumour are essential.

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Background

Osteoblastomas and aneurysmal bone cysts (ABCs) each comprise 1% of primary bone tumours.[1,2]

Osteoblastomas were first clearly defined by Lichtenstein in 1956, as a benign bone tumour of osteoblastic derivation, other than an osteoid osteoma.[3] Osteoblastomas, which comprise 3% of all benign bone tumours, are most common in young males and frequently arise on the vertebrae or long bones. Its characteristic pathological findings include a well-vascularised, osteoblastic connective-tissue stroma in which osteoid and new bone trabecula are deposited.

ABCs were first described by Jaffe and Lichtenstein in 1942, and subsequent reports were made by both of these authors.[4] Only 3% of ABCs are found in the head and neck, with the most common location being the mandible. ABCs are benign, thin-walled, blood-filled cavities that arise either primarily, or in association with other bone lesions. Primary and secondary ABCs differ with respect to their neoplastic mechanisms.[2] Primary ABCs are associated with increased expression of oncogenes USP6 and CDH11, which are absent in secondary ABCs. Secondary bone cysts form as a result of osteolysis following haemorrhage. Haemorrhage in turn results from a tumour-induced increase in venous pressure.

As both osteoblastomas and ABCs are uncommon clinical entities, especially in calvaria, an osteoblastoma accompanying a secondary ABC of the calvaria is quite rare. Only three cases describing a secondary ABC in the setting of a calvarial osteoblastoma can be found in the literature.[5–7]

Case description

The patient, a 24-year-old male, presented to our clinic with a 2-year history of a painless lump in the hair-bearing region of the left fronto-parietal area. He had no history of trauma, surgery or infection of the affected area. The patient's medical history was unremarkable. He had an eight-pack-year smoking history. He had no history of exposure to environmental carcinogens. He denied headache, dizziness and/or nausea. The hemispherical, 6-cm mass was non-tender, and no deficits or other abnormalities were present on neurologic exam. The tumour had the hardness of bone and no pulsation, bruit or Tinel-like sign was evident. While the tumour was immobile on the skull, the scalp moved freely over it. The laboratory studies were unremarkable.

Computed tomography (CT) demonstrated a well-circumscribed 53 × 38 × 43-mm homogenous hypodense tumour in the diploic space of the left fronto-parietal bone (Figure 1). The continuity of both the outer and inner tables of the skull was maintained in spite of the cortex being thinned.

3.0-T T1-weighted magnetic resonance imaging (MRI) showed a well-circumscribed, intradiploic, multilocular, cystic tumour. The tumour displaced the brain parenchyma without midline shift. The underlying dura mater and brain parenchyma showed no signal intensity change. Neither brain oedema nor hydrocephalus was noted. The overlying subcutaneous tissue appeared normal. A gadolinium-enhanced fat-suppressed T1-weighted gradient-echo sequence showed strong peripheral and septal enhancement of the tumour (Figure 2). Signal-intensity change suggesting intraosseous horizontal extension of the tumour was not evident.

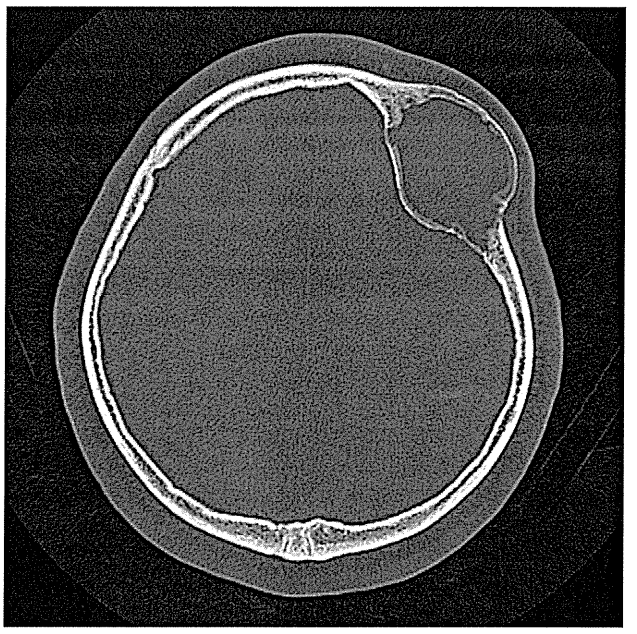

Figure 1 Preoperative computed tomography without contrast medium showing a well-demarcated, intradiploic mass of the frontal and left parietal bone. The inner and outer cortical plates are maintained despite thinning.

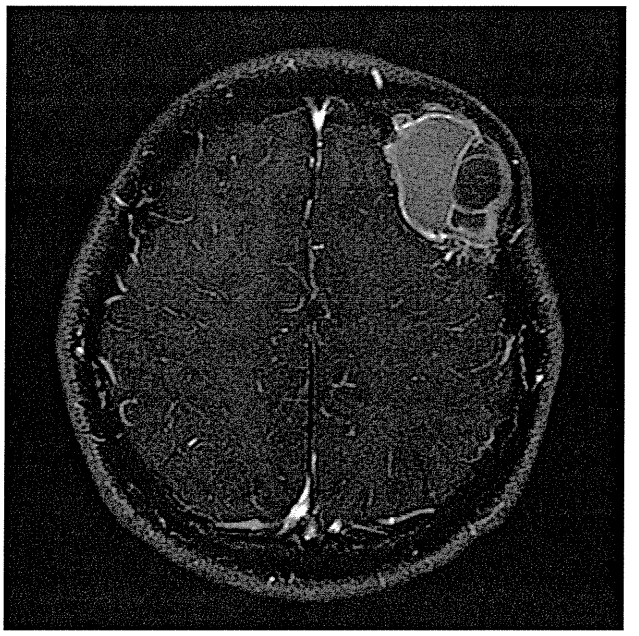

Figure 2 Preoperative 3.0-T magnetic resonance imaging. Gadolinium enhanced fat-suppressed T1-weighted gradient-echo sequence shows a well circumscribed, intradiploic, multilocular, cystic tumour with marginal and septal enhancement of the tumour.

A hypodense, homogenous intradiploic tumour with maintained outer and inner tables of the skull in spite of substantial enlargement on CT is the essential diagnostic point of the osteoblastoma. A well-defined multilocular bone cyst with an underlying bone tumour on MRI is consistent with the diagnosis of the secondary aneurysmal bone cysts. Based on these findings, we diagnosed the tumour as an osteoblastoma associated with secondary ABC preoperatively.

Surgical procedure

An *en bloc* tumour resection with a 10-mm horizontal margin and simultaneous reconstruction using an autologous calvarial bone graft was planned. The tumour was easily exposed through a coronal incision with no adhesion to the scalp. It was dark red—purple in colour with a bony protrusion of about 50 mm in diameter. It straddled the frontal and left parietal bones. The calvarium adjacent to the tumour appeared normal in colour and texture. The resection margins were outlined as a 70 × 70-mm quadrangle. After boring burr holes at the corners of the planned quadrilateral resection line, we completely resected the tumour including the outer and the inner table of the skull above the dura mater. The tumour separated easily from the dura with scant bleeding. Macroscopically, both the inner and the outer tables of the tumour were maintained in spite of thinning and there were no findings suggesting fenestration. The calvarial defect measured 73 × 69 mm. There was no evidence of dural injury. To cover the craniectomy defect, we harvested a full-thickness calvarial bone graft measuring 70 × 70 mm from the right fronto-parietal bone. We separated the outer plate and inner plates of the bone graft and used one plate for the tumour-site defect and the other to close the defect created when the graft was harvested. The bone grafts were fixed to the surrounding bones with absorbable plates and screws (Figure 3).

The postoperative course was uneventful. CT performed 3 months after the operation showed improvement of the brain parenchymal shift. There was no evidence of recurrence 2 years postoperatively.

Pathological findings

The tumour measured 50 × 47 × 30 mm in size. The cut surface of the tumour demonstrated multiple chambers separated by thin bony membranes. The chambers contained serous brown fluid.

Low-power microscopic examination of a haematoxylin—eosin stained section demonstrated a distinct border between the tumour and the normal bone (Figure 4). The cyst wall consisted of small trabecular areas and dense stromal cells. There was a zonation where the bone trabeculae decreased in size and the stroma became more cellular proximal to the cyst cavity. On high-power microscopic images, the tumour showed a fine trabecular pattern with the trabeculae rimmed by osteoblasts and scattered osteoclasts. The stroma was hypercellular in comparison to the normal bone. The stroma consisted of spindle cells and thin-walled microvessels. The pathologic diagnosis was of an osteoblastoma with a secondary ABC.

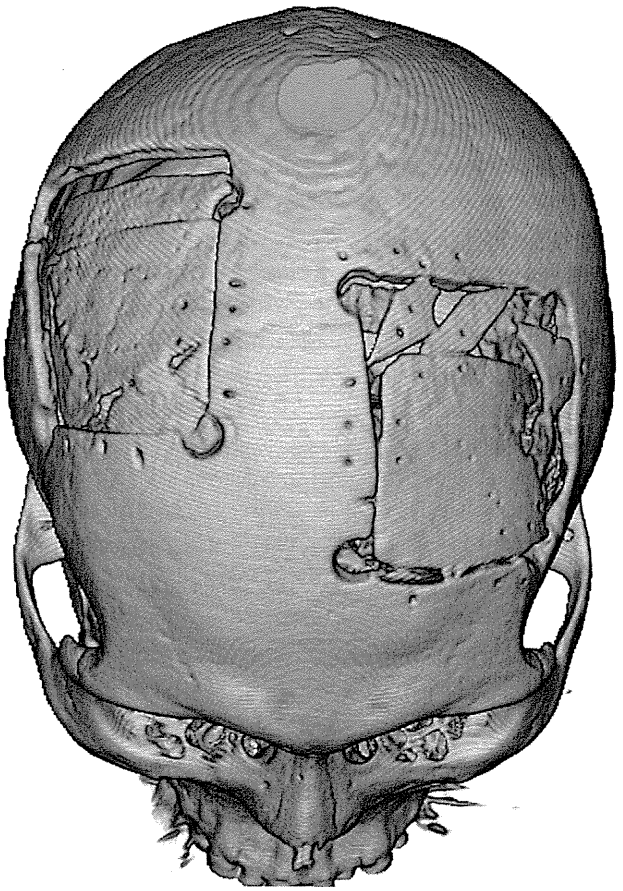

Figure 3 Computed tomography three months after the operation. The defect resulting from the tumour resection is covered by a calvarial bone graft harvested from the right fronto-parietal bone.

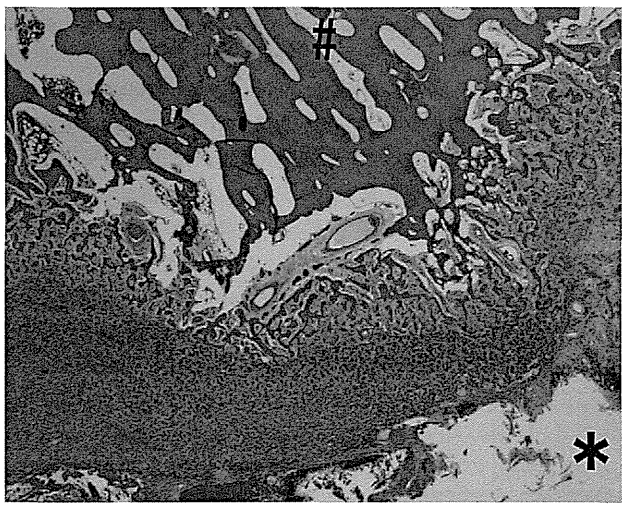

Figure 4 Pathological findings of the tumour. Low-power image showing the fine trabeculae, which composed the tumour wall, and the osteoid consisting of the hypercellular stroma. Zonation, that trabeculae decreases in size and the stroma becomes more cellular, is present in a peripheral to central direction. # indicates normal bone surrounding the tumour. * indicates cavity of the aneurysmal bone cyst.

Discussion

On CT, the calvarial osteoblastoma often appears as an osteolytic lesion with enlarged diploe, a variably present egg-shell-like thin outer and inner tables and varying degrees of calcification.[1] As seen in our case, the preservation of continuity of both the outer and inner tables surrounding the tumour, in spite of thinning, is consistent with the tumour being benign.

T-1 weighted MRI of osteoblastomas typically shows low or isointensity.[1] In our case, different intensities were present with distinct borders, consistent with a multilocular tumour. T-2 weighted MRI shows iso- or high intensity. Gadolinium-enhanced fat-suppressed T1-weighted MRI shows strong enhancement reflecting the rich vascular supply of the tumour. In the present case, the septum and the peripheral wall corresponding to the main body of the osteoblastoma demonstrated strong enhancement.

In our case, the secondary ABC occupied a large portion of the tumour volume. As a result, the osteoblastoma component existed only in the peripheral wall and septum. The zonation where the bone trabeculae decreased in size and the stroma became more cellular proximal to the cyst cavity was observed in our case. We think it was a consequence of increased intracystic pressure of the ABC and following condensation of the surrounding osteoblastoma component around the cyst.

Only three cases of calvarial osteoblastoma with secondary ABC have been reported.[5–7] Similar to our case, complete surgical resection was performed uneventfully in a case of frontal and a case of occipital osteoblastoma with secondary ABC.[5,7] However, there was a case of huge osteoblastoma with ABC of the skull base involving the sellar mass, optic foramen and optic chiasma, in which total resection of the tumour was difficult and the tumour recurred after the operation.[6]

In terms of the differential diagnosis, osteoidosteoma, giant cell tumour and osteoblastic osteosarcoma sometimes resemble osteoblastoma in its histology especially with a small biopsy specimen.[3] However, it is usually easy to diagnose an osteoblastoma preoperatively because clinical settings and image findings are quite different from each other.

With respect to the treatment of osteoblastoma of the calvarium, Lichtenstein recommended curettage or resection without a wide margin.[3] In our opinion, curettage is inappropriate as the tumour will likely recur. Others have argued that complete excision with a narrow margin is sufficient to prevent recurrence. Abnormal intensity change of the diploic space beyond the bony protuberance by the tumour will, however, make the surgical margin difficult to identify.[8] In our case, abnormal signal intensity of diploe was not evident; hence, it was easy to determine the tumour border.

Few reports are available addressing reconstruction with autologous bone grafts of defects following calvarial osteoblastoma resection.[1] Resin or artificial bone is used in other reports.[8–10] In our case, we elected to use the calvaria as a bone-graft donor site because we think autologous bone graft is superior to bone substitutes in terms of long-term safety.

Ethical approval

Not required.

Funding

None.

Conflicts of interest

None declared.

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家族性LCAT欠損症

SUMMARY

レシチン-コレステロールアシルトランスフェラーゼ（LCAT）欠損症は，LCAT酵素の先天的機能異常によって引き起こされる難治性の常染色体劣性疾患である．LCATの触媒する遊離コレステロールのエステル化や，それに伴いコレステロールの肝臓への逆転送が障害される．

HDLのエステル化活性とLDLのエステル化活性の両方を欠損する家族性LCAT欠損症（FLD, OMIM #245900）とHDLのエステル化活性のみ欠損する魚眼病（FED, OMIM #136120）という2つの病態に大別される．

臨床症状は，低HDL血症，角膜混濁，さらにFLDは貧血を伴う．FLDは腎機能障害が認められ，予後不良の症例では腎不全を合併する．

現在までに原因となる遺伝子変異は80種類以上同定されている．

代謝障害と病態

LCATは主にHDL上でアポリポタンパクA-Ⅰ（アポA-Ⅰ）を共役因子として存在し，HDLの遊離コレステロールのエステル化による成熟に必要である．LCATが機能することで，末梢組織からの遊離コレステロールの引き抜きが促進される[1]．したがって，LCAT活性の低下・欠損によりHDLの成熟が障害され，血中にdiscoidal HDL粒子が出現する（**図1**）．HDLコレステロールは著減し，それとともにアポA-Ⅰ，A-Ⅱが低下する．本症は角膜混濁，腎機能障害，貧血を主徴とするが，これらはLCAT活性の異常により遊離コレステロールやレシチン（ホスファチジルコリン）が増加し，組成の変化したリポタンパクが組織に沈着することに起因する．

FLDとFEDともに，幼少期より角膜混濁が出現することが特徴的である．FLDでは赤血球膜の脂質組成異常により標的赤血球が出現し，貧血が認められる．腎機能障害の程度は，無症状から腎不全に至る症例までさまざまである．FLDではLDL分画に異常リポタンパク（LpX）が検出される．LpXは脂肪制限食により低下し，腎機能障害の程度と関連しているという報告がある．腎不全などの合併症の進展は食事などの環境因子による修飾を受ける．さらに，FLDの遺伝子変異やアポE遺伝子型が，異常リポタンパクの出現[2]や冠動脈疾患のリスクに関与するとする報告がある．

臨床病型

HDLのエステル化活性（α活性）とLDLのエステル化活性（β活性）の両方を欠損するFLDと，HDLのエステル化活性のみ欠損するFEDという2つの病態に大別される（**表1**）．FLDのなかには，血中にLCATタンパクが存在しないものと不活性酵素が残存するものがある．活性が部分的に残存する変異も知られている．複合ヘテロ接合体患者も報告され，その病態は多様性を示す．

診断

①一般検査：血中HDLコレステロール値が低下する．これまでの症例報告をまとめると，ほとんどの症例は10 mg/dL未満である．LCAT変異ヘテロ接合体も健常より低値を示し，一般の低HDL血症の原因の一つとなる[3]．コレステロールエステル化率（CE/TC）はFLDで減少し，FEDは大きく低下することはない．眼科所見の角膜混濁が特徴的であり，FEDでより顕著である．FLDはほとんどで貧血が認められる．FLDは病態の進行に伴いタンパク尿が出現する．3歳でタンパク尿が出現した症例も報告されている．

②特殊検査：アポA-Ⅰ，A-Ⅱが著しく減少する．リポタンパクの電気泳動解析（アガロース，ポリアクリルアミド）で，LDL分画を中心とした異常リポタンパク（IDL, LpX）を同定，血清または血漿中LCAT活性を測定する．肝臓が産生する酵素であることから，重篤な肝障害でLCAT活性が低下するので鑑別が必要である．FLDが疑われる場合は腎生検が有用であ

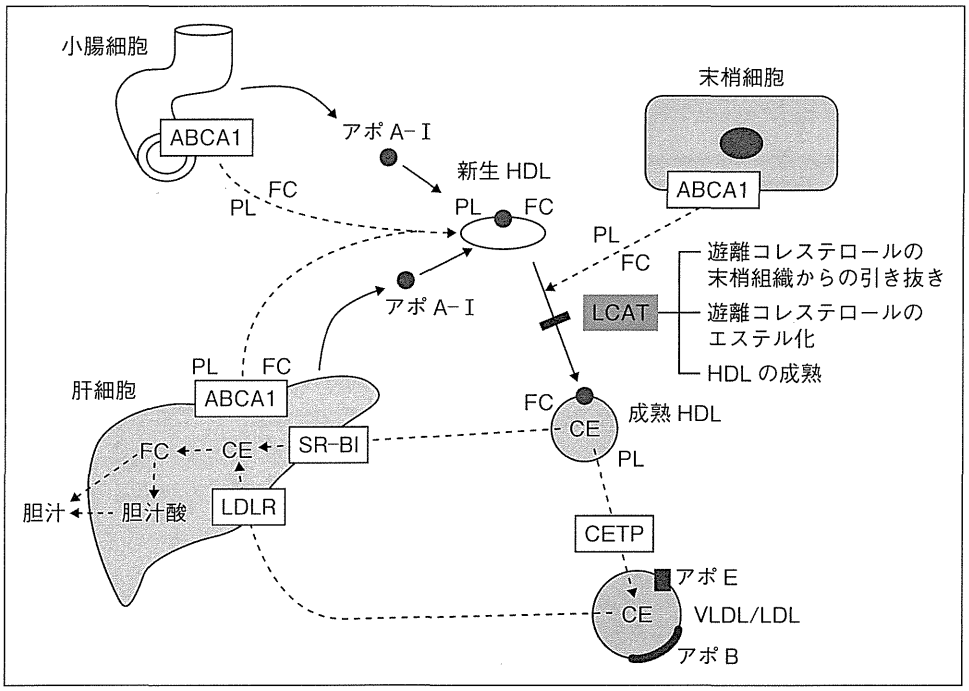

図1　LCAT の生理機能とコレステロール逆転送系

遊離コレステロール（FC）やリン脂質（PL）は ABCA1 輸送タンパクを介して肝細胞と小腸細胞から排出され，アポ A-Ⅰと結合，新生 HDL が生成される．他の末梢組織から抜き取られた FC や PL が新生 HDL に抱合され，LCAT がこれらを基質としコレステロールエステル（CE）を生成し，HDL が成熟する．HDL で生成された CE はスカベンジャー受容体クラス BI（SR-BI）を介して，またはコレステリルエステル転送タンパク（CETP）によって VLDL や LDL に転送された後，LDL 受容体（LDLR）を介して肝細胞に取り込まれ，FC，胆汁酸に変換され胆汁中に排泄される．

表1　FLD と FED の臨床所見

臨床所見	FLD	FED
角膜混濁	○	○
貧血	○	
腎障害	○	
HDL-C	↓↓	↓↓
CE/TC	↓↓	↓
アポ A-Ⅰ	↓↓	↓
アポ A-Ⅱ	↓↓	↓
LCAT α活性	↓↓	↓↓
CER	↓↓	↓

○：認められる
↓：減少
↓↓：著しく減少

る．糸球体基底膜へ遊離コレステロールやリン脂質が沈着している．

③確定診断：上記の検査に加えて遺伝子解析を行う．末梢単核球より DNA を抽出し，LCAT 遺伝子領域の塩基配列を検索する．劣性遺伝形式をとることから，両親と患者に同一の変異が同定される．これまで，80 種類以上の遺伝子異常が報告されている．

治療，予後

FLD の生命予後を規定する因子は腎不全の進行である．40～50 歳以降に人工透析や腎移植が必要となる例が多い．幼少期から重篤になるケースは報告されていない．腎機能障害のある症例は，腎機能の保護を目的として，低脂肪食による食事療法，アンギオテンシンⅡ受容体拮抗薬，アンギオテンシン変換酵素阻害薬などの薬物療法が行われている．いずれも対症療法であり，進展予防効果や再発の可能性は明らかでない．

新鮮血漿の輸血により病態が改善することが報告されている．根治療法として，リコンビナント LCAT の持続補充療法が期待されている．その方法として，組換えタンパク製剤[4]と遺伝子細胞治療の臨床研究[5]が米国と日本で進められている．

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