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CASE REPORT

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Plasma cell myeloma of the skull base: report of two cases

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Abstract Plasma cell myeloma (PCM) of the skull base is rarely encountered in neurosurgical practice. PCM has a wide spectrum of pathology, including a quite benign, solitary plasmacytoma (SPC), and an extremely malignant, multiple myeloma (MM) at the two ends of the spectrum. We have described two patients with PCM of the skull base, of which one harbored SPC, and the other progressed to MM. In case 1, a 46-year-old man presented with left multiple cranial nerve impairments and had a large skull base tumor. Subtotal removal was performed. The specimen and general examination, including bone marrow aspiration, revealed SPC. Postoperatively 50 Gy of external radiotherapy was administered. The patient has no manifestation of MM 24 months after the initial presentation. In case 2, a 53-year-old woman presented with left abducens palsy and had a left petroclival osteolytic mass. Gross total resection was performed. The specimen revealed a plasmablastic tumor, i.e., myeloma. General examination established the diagnosis of MM. She was administrated adjuvant chemotherapy and autologous bone marrow transplantation. She is alive without local recurrence 30 months after the initial presentation.

Key words Plasma cell myeloma · Solitary plasmacytoma · Multiple myeloma · Proliferation indices · Crystalloid inclusion

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Introduction

Plasma cell myeloma (PCM) of the skull base is rarely encountered in neurosurgical practice. It is classified according to its biological behavior and histopathological features into a benign type, solitary plasmacytoma (SPC), and a malignant type, development of multiple myeloma (MM).

SPC of the skull base without the development of MM is extremely rare; only seven cases have been reported.[1–7] In these previously reported cases of skull base SPC, MM was not excluded by a sufficient follow-up period.

We describe two patients with PCM of the skull base, of which one harbored SPC and the other progressed to MM. The former demonstrated amyloid deposits and crystalloid inclusions microscopically. These features in PCM of the skull base have not previously been reported. We present them with special reference to the prognostic significance of precise histopathological examination.

Case report 1

Clinical summary

A 46-year-old man presented with hearing disturbances on the left and gait instability. He developed left-side facial palsy, abducens palsy, and facial hypesthesia within a month. Additionally, he complained of hoarseness, nuchal pain, and head instability.

Magnetic resonance imaging (MRI) revealed a large skull base tumor with osteolytic involvement of the clivus, bilateral petrous apex, sphenoid sinus, and the atlantoaxial joint. The lesion was enhanced heterogeneously with gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA) (Fig. 1A and B). Bone-window computed tomography (CT) scanning showed erosion of the bilateral petrous apex and involvement of the left internal acoustic meatus (Fig. 1C). Angiography demonstrated the feeding arteries arising from the left vertebral artery (Fig. 1D). The physical exami-

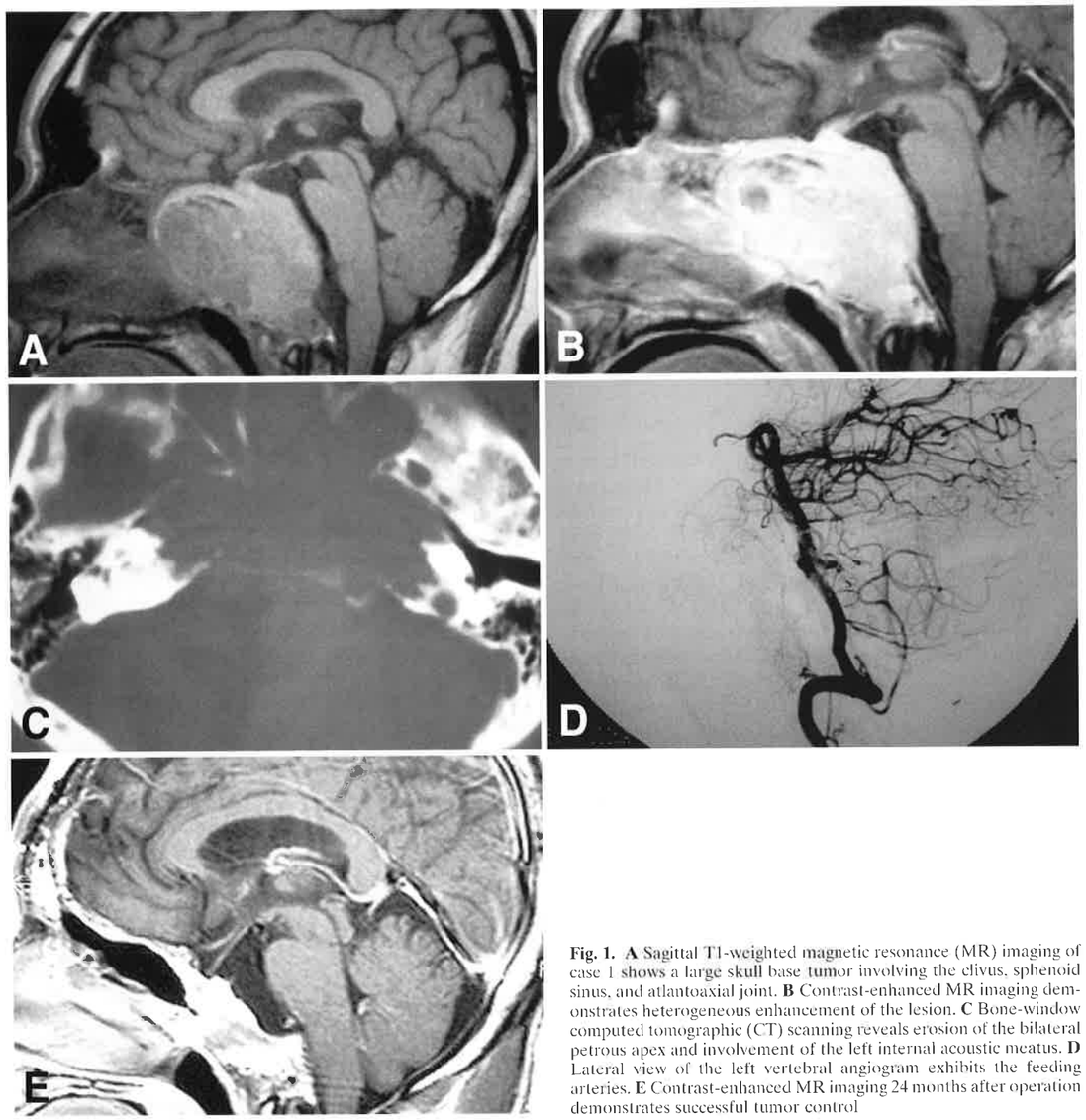

Fig. 1. **A** Sagittal T1-weighted magnetic resonance (MR) imaging of case 1 shows a large skull base tumor involving the clivus, sphenoid sinus, and atlantoaxial joint. **B** Contrast-enhanced MR imaging demonstrates heterogeneous enhancement of the lesion. **C** Bone-window computed tomographic (CT) scanning reveals erosion of the bilateral petrous apex and involvement of the left internal acoustic meatus. **D** Lateral view of the left vertebral angiogram exhibits the feeding arteries. **E** Contrast-enhanced MR imaging 24 months after operation demonstrates successful tumor control

nation findings and laboratory data were within normal limits.

The patient underwent surgical resection by the extended basal frontal epidural approach. The dura mater remained intact, but tumor removal was subtotal, because the tumor around the atlantoaxial joint was impossible to remove. All cranial nerve impairments improved gradually within a few days after the operation. Bone marrow aspiration, serum and urine protein electrophoresis for evaluation of monoclonal gammopathy, and skeletal survey showed no manifestation of MM. He was administered adjuvant external beam radiotherapy of 50 Gy. A close follow-up examination revealed no manifestation of MM, and the tumor had been controlled successfully up to 26 months after the initial presentation (Fig. 1E)

Pathological findings

Hematoxylin and eosin (H&E)-stained sections demonstrated two cell patterns: dense small round cells with small pleomorphic hyperchromatic nuclei and dense medium-

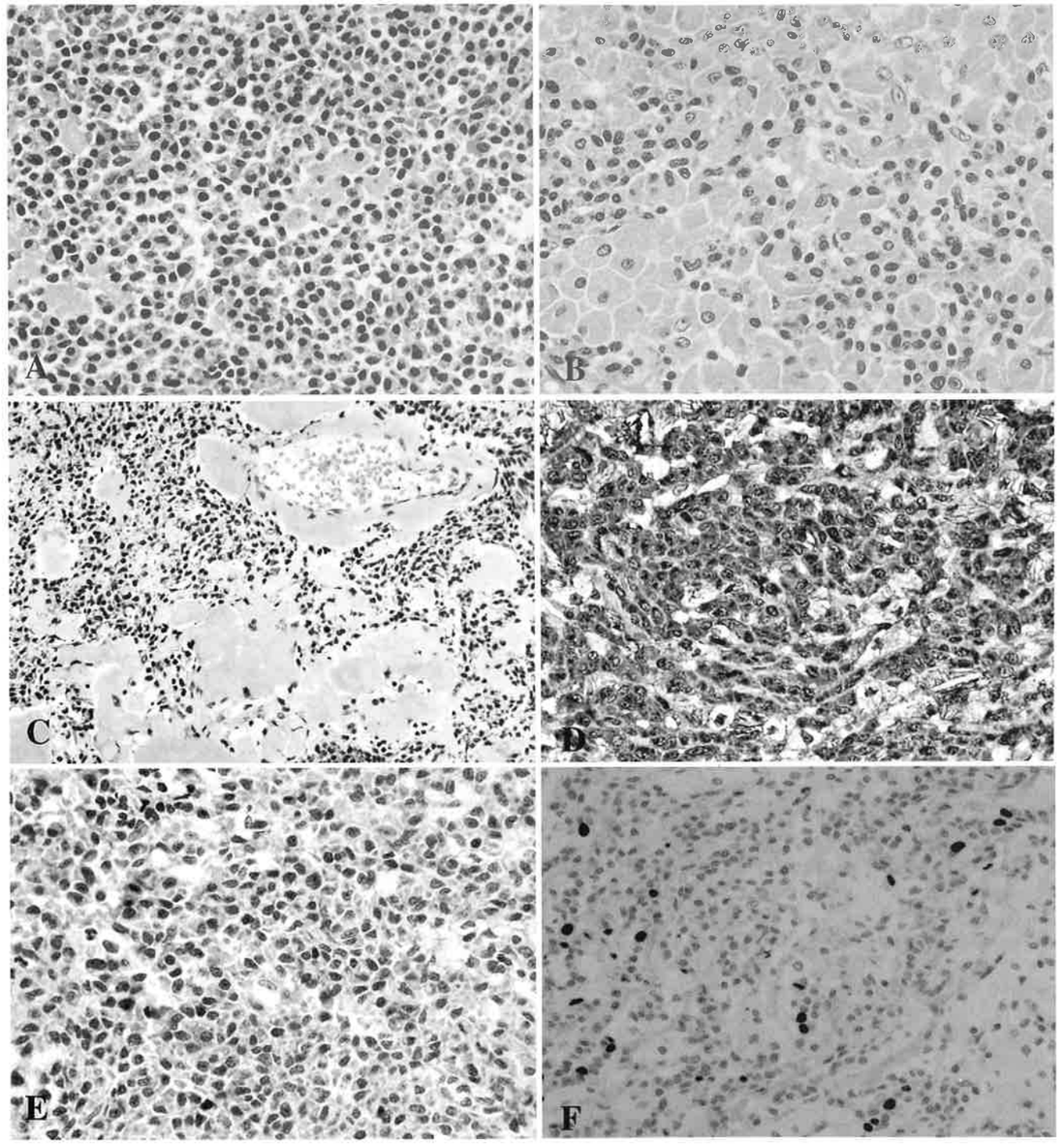

Fig. 2. **A** Photomicrographs of hematoxylin and eosin (H&E)-stained sections reveal dense atypical plasma cells with hyperchromatic eccentric nuclei and eosinophilic cytoplasm. Most of them exhibit moderate nuclear atypism. H&E, original magnification ×200. **B** Most tumor cells have abundant cytoplasm with eosinophilic crystalloid inclusions. H&E, original magnification ×400. **C** Scattered intercellular amyloid deposits and massive deposits in vessel walls are seen. Crystalloid inclusions are also stained with Congo Red. Congo Red, original magnification ×200. **D** Immunohistochemistry of the κ-chain reveals the diffuse positive cytoplasm of tumor cells. Original magnification ×400. **E** Immunohistochemistry of the λ-chain reveals the negative cytoplasm of tumor cells. Original magnification ×400. **F** MIB-1 labeling index is 2% (0%~4%). Original magnification ×200

sized cells with crystalloid inclusions in the cytoplasm (Fig. 2A and B). Massive amyloid deposition was seen intercellularly and in the vessel walls with Congo Red staining (Fig. 2C). Immunohistochemistry revealed the existence of the kappa chain (Fig. 2D) and the absence of the lambda chain (Fig. 2E), which proved the cells to be atypical plasma cells producing monoclonal gammopathy. The MIB-1 labeling index, representing the percentage of positively stained

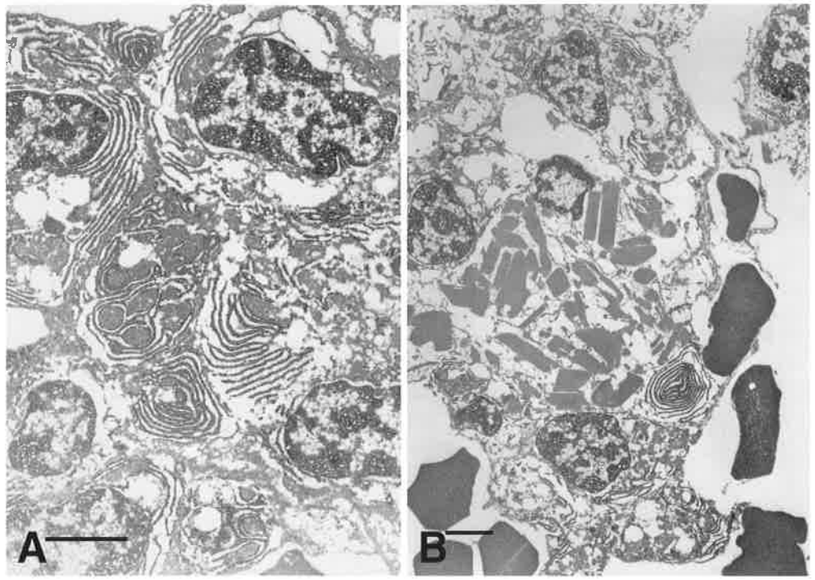

Fig. 3. Ultramicroscopic study. **A** Most of the tumor cells exhibit a laminated or whorl arrangement of the rough granular endoplasmic reticulum. Original magnification × 5000. *Bar* = 4 μm. **B** Crystalloid inclusions are seen in a tumor cell. Original magnification ×3000. *Bar* = 4 μm

tumor cell nuclei, was 2% (0%~4%) (Fig. 2F). Electron micrography revealed a laminated, whorl arrangement of the rough granular endoplasmic reticulum and crystalloid inclusions (Fig. 3A and B).

Case report 2

Clinical summary

A 53-year-old woman presented with diplopia. Neurological examination revealed left abducens palsy on admission. A left petroclival osteolytic mass involving the left internal carotid artery was shown by MRI. The tumor was enhanced homogeneously with Gd-DTPA (Fig. 4A and B). Bone-window CT scanning demonstrated erosion of the left petrous apex and the clivus (Fig. 4C). Angiography revealed feeding arteries arising from the left carotid artery (Fig. 4D).

The patient underwent surgical resection by the anterior epidural transpetrosal approach one month after admission. Gross total resection was performed. The left abducens palsy improved gradually after the operation. Further examination, including bone marrow aspiration and general survey, established the diagnosis of MM. She received adjuvant chemotherapy and autologous bone marrow transplantation. The local tumor had been controlled successfully up to 30 months after operation (Fig. 4E).

Pathological findings

H&E-stained sections demonstrated a sheet of small round cells with highly pleomorphic nuclei and a high nucleus/cytoplasm ratio (Fig. 5A and B). Immunohistochemistry revealed the existence of the kappa chain (Fig. 5C) and the absence of the lambda chain (Fig. 5D), which proved the cells to be atypical cells producing monoclonal gammopathy. The tumor cells were positive for CD79a antibody, which represented B cell lymphoma with differentiation to plasma cells (Fig. 5E). The MIB-1 labeling index was 15% (5%~20%) (Fig. 5F). These findings indicated a diagnosis of myeloma rather than plasmacytoma.

Discussion

In radiological findings, PCM of the skull base is difficult to differentiat from other osteolytic skull base tumors, including meningiomas, chordomas, metastatic carcinomas, and nasopharyngeal carcinomas. It is also difficult to differentiate PCM histologically from other small round-cell tumors, including malignant lymphomas, esthesioneuroblastomas, and plasma cell granulomas. As shown in this report, PCM of the skull base has a wide spectrum of pathology from quite benign to extremely malignant at the two ends of the spectrum. We emphasize that precise histopathological examination is important to assess the prognosis as well as to establish an accurate diagnosis. We discuss mainly the prognostic indicators of PCM of the skull base.

The indicator of a poor outcome of PCM is a progression to MM, which results in a fatal course. Previously reported prediction indicators of progression to MM are intramedullary nature, the existence of residual tumor, and location in the skull base.[8–11] Sixty to seventy percent of intramedullary lesions arising from the bone progress to MM, compared with 10% to 20% of extramedullary lesions arising from the

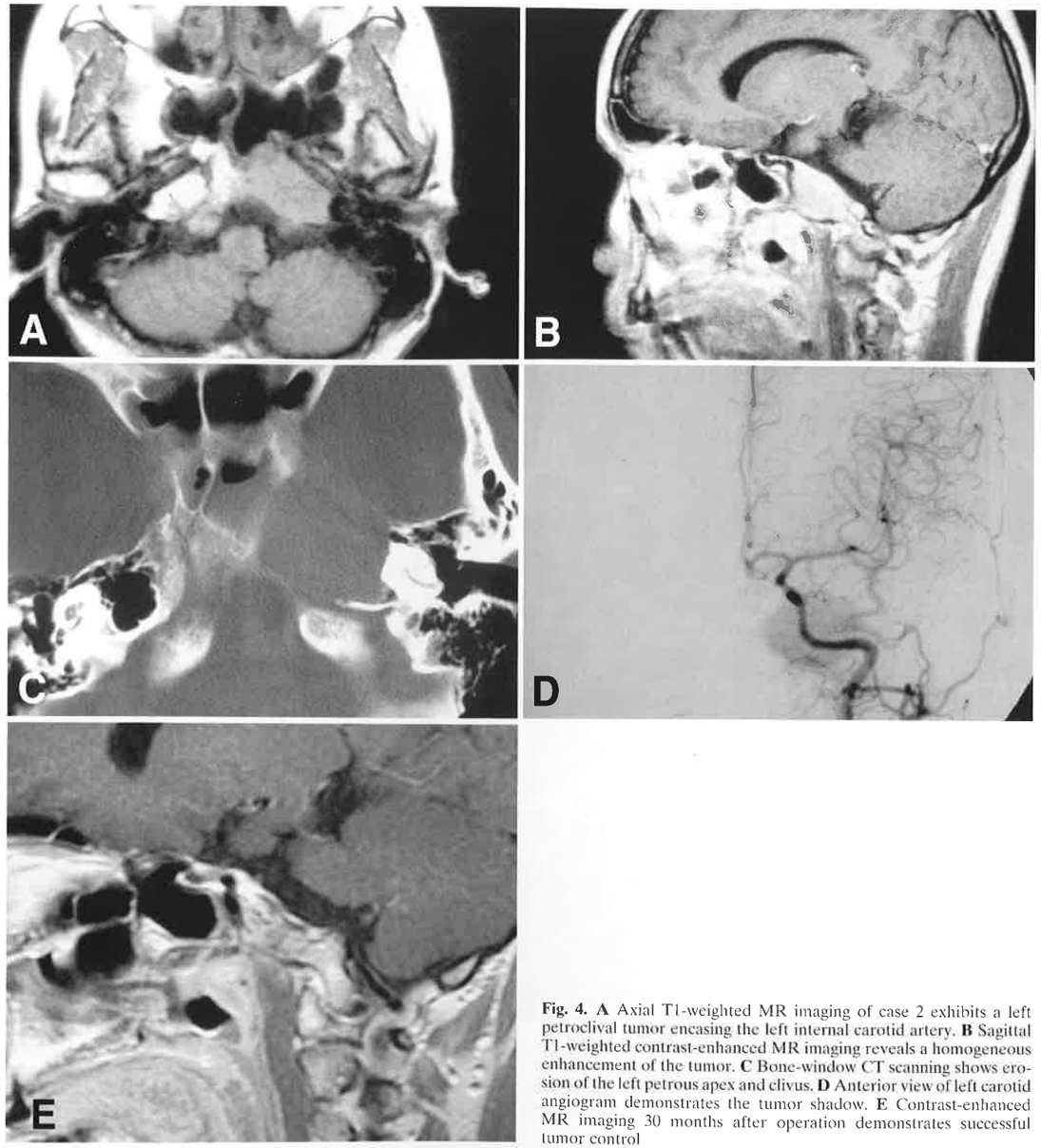

Fig. 4. **A** Axial T1-weighted MR imaging of case 2 exhibits a left petroclival tumor encasing the left internal carotid artery. **B** Sagittal T1-weighted contrast-enhanced MR imaging reveals a homogeneous enhancement of the tumor. **C** Bone-window CT scanning shows erosion of the left petrous apex and clivus. **D** Anterior view of left carotid angiogram demonstrates the tumor shadow. **E** Contrast-enhanced MR imaging 30 months after operation demonstrates successful tumor control

soft tissues, such as the mucosal linings of the middle ear, mastoid air cells, and paranasal sinuses.[9–12] According to the previous case reports, many of the skull base lesions that were initially considered to be solitary eventually progressed to MM. These suggest that most PCMs of the skull base are of intramedullary nature and are actually in the early stage of MM.[4,8,10,11] On the contrary, PCMs of the other cranial locations are mostly of extramedullary nature and appear to be SPC.[5,8,10,12–14] Because of this wide variety of pathology, it is important to identify the original site of the tumor, intramedullary or extramedullary. However, this is often difficult, especially in a large skull base lesion like that in the present case 1.

In addition to the original site of the tumor, we advocate that plasmablastic features, including pleomorphism, mitosis, and multinucleated cells,[15] and higher proliferation indi-

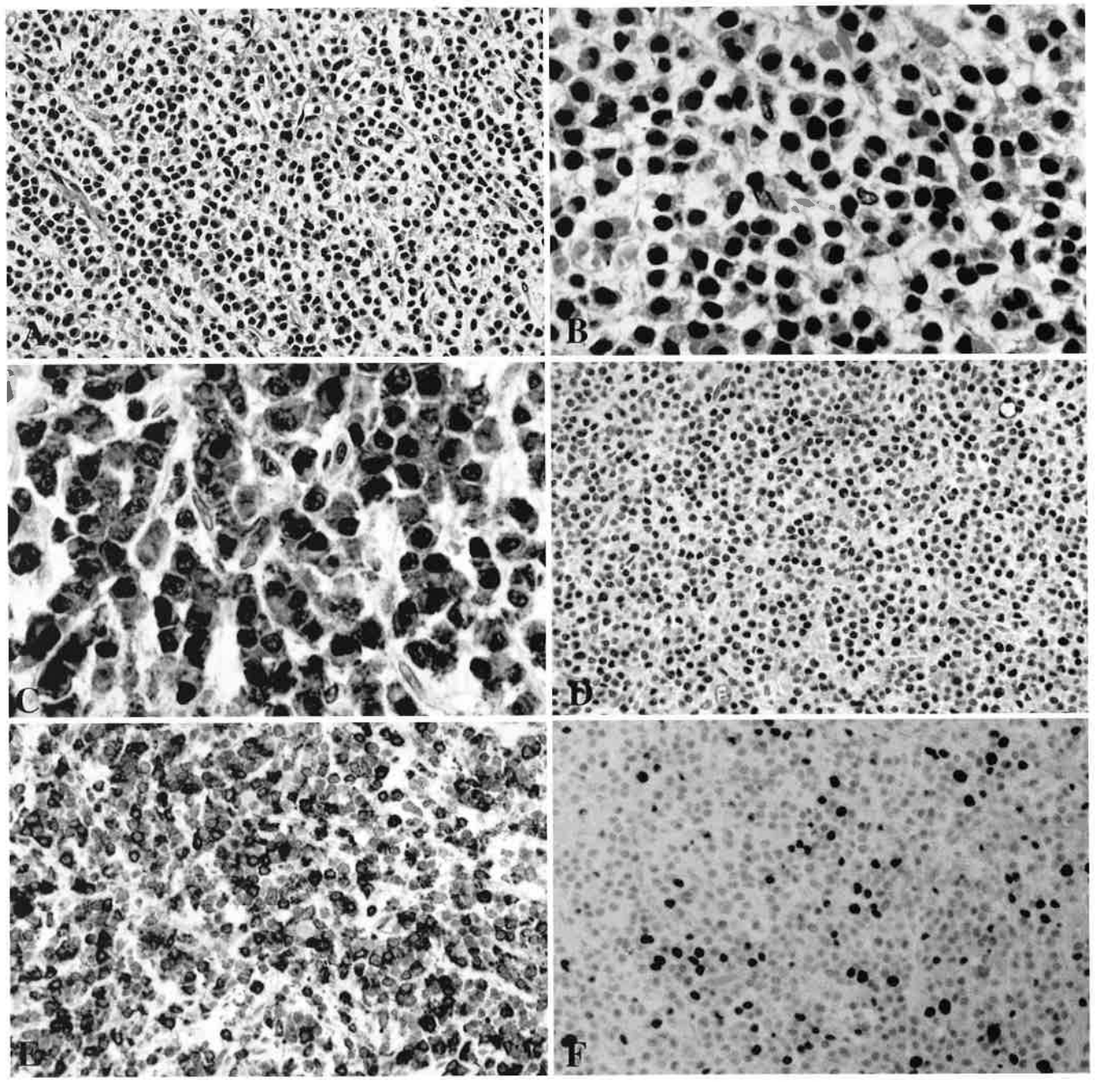

Fig. 5. **A** H&E stained sections demonstrate a sheet of small round cells. Original magnification ×400. **B** Tumor cells with highly pleomorphic nuclei and high nucleus/cytoplasmic ratio. Original magnification ×1000. **C** Immunohistochemistry reveals the existence of the κ-chain. Original magnification ×1000. **D** Immunohistochemistry reveals the absence of the λ-chain. Original magnification ×400. **E** The tumor cells are positive for CD79a antibody. Original magnification ×400. **F** MIB-1 labeling index is 15% (5%~20%). Original magnification ×400

ces by MIB-1 or Ki-67 labeling,[11] are important prognostic indicators. By contrast, intratumoral amyloid deposits and crystalloid inclusions suggesting mild proliferation of neoplastic plasma cells are considered to be benign features and are often noticed in extramedullary PCM. These histopathological features are encountered in about 24% of SPCs of the respiratory tract.[16] These are also reported in other cranial locations,[14,17] but have not previously been found in PCM of the skull base.

The optimal treatment of PCM is complete surgical resection followed by postoperative external radiotherapy.[8,10,11] Some authors have demonstrated that only radical excision prevented both tumor recurrence and progression to MM in cases of PCM in other cranial locations.[13,18] However, in a large skull base lesion, because of the restriction of the operative field, complete resection is often impossible. In some previous cases, only biopsy and radiation therapy resulted in benign clinical courses.[3,6,14,17]

Therefore, adjuvant radiation therapy is advisable, even in cases under consideration for total resection.

Skull base lesions of possible extramedullary origin and with benign histopathological features have an increased chance of having SPC. Bindal et al. have proposed that a diagnosis of SPC can be established and the possibility of later progression to MM may be excluded in patients who do not develop MM in the early postoperative period.[8] On the other hand, Schwartz et al. have emphasized that the diagnosis should be established at least one year after the initial presentation.[11] By contrast, skull base lesions that are considered to be of intramedullary origin and that demonstrate histopathological plasmablastic features have a grater chance of developing into MM. Even if a skull base lesion is considered to be SPC, a close follow-up examination is required for the early detection of possible progression to MM. In any cases in which MM has eventually developed, chemotherapy should be started as early as possible after the establishment of this diagnosis.

In summary, we have presented two PCMs of the skull base: one SPC and the other development of MM. PCM has a wide spectrum of pathology, which eventually determines the prognosis. The poorest outcome is progression to MM. Prediction indicators of this progression have been considered to be intramedullary nature, the existence of residual tumor, and location in the skull base. In addition to these, we emphasize that histopathological plasmablastic features and higher proliferation indices are other important prognostic indicators. Precise histopathological examination is important to assess the prognosis as well as to establish an accurate diagnosis.

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