CASE REPORT

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Sinonasal Undifferentiated Pleomorphic Sarcoma in Five Patient Cases

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Undifferentiated pleomorphic sarcoma (UPS) is a rare soft tissue sarcoma of the sinonasal area. Here, we present two primary cases of UPS and three post-irradiation sinonasal UPS cases. Imaging findings were misinterpreted by radiologists as representing other malignant tumors or recurrence of the primary tumor. Our cases indicate that post-irradiation UPS can originate within any part of the radiation field. Treatment outcomes of primary sinonasal UPS seem to be favorable if the tumor is treated aggressively, but the outcomes of post-irradiation sinonasal UPS may be poor if appropriate surgical margins cannot be obtained.

KEY WORDS: Undifferentiated pleomorphic sarcoma · Paranasal sinus · Nasal cavity · Radiation.

INTRODUCTION

Undifferentiated pleomorphic sarcoma (UPS), previously considered as a malignant fibrous histiocytoma, is the most common soft tissue sarcoma in adults.[1] UPS was recognized by O'Brien and Stout in 1964 as a clinico-pathologic entity, i.e., a pleomorphic sarcoma that contains both fibroblast-like and histiocyte-like cells in varying proportions, arranged in a storiform pattern. UPS occurs most commonly in the extremities and central body but has been reported to occur in other sites. In rare cases, UPS originates from the head and neck region, most commonly from the sinonasal tract.[2]

In addition, UPS occurs secondarily to radiation, trauma, and benign bone tumors. Imaging findings of UPS are rather nonspecific, shown as soft tissue invasion and bone destruction, making them difficult to distinguish from pre-existing malignant conditions, fibrous tumors, and inflammatory conditions.[3] Here, we report five cases of primary or secondary UPS of the sinonasal area.

CASE PRESENTATIONS

The clinical characteristics of our cases are shown in Table 1. Two male patients and three female patients were included. Their ages at diagnosis ranged from 30 to 58 years (median of 47 years). The most common symptom was nasal obstruction followed by pain, epistaxis, and cheek swelling. Upon physical examination, an infiltrative mass or swelling was found in the affected area. Lymph node or distant metastasis was not found at diagnosis. Histologically, all five cases were diagnosed as storiform-pleomorphic subtype. The tumors showed fibroblast-like and histiocyte-like cells arranged in a storiform pattern at least in some areas. Atypical giant cells and inflammatory cells were common. Mitotic activity and nuclear atypia varied greatly among the different cases.

Two cases (cases 1 and 2) were primary UPS of the maxillary sinus without a history of radiation or trauma. They were found at T2 (tumor > 5 cm in the greatest dimension). Radiologic studies have shown soft tissue mass in the maxillary sinus with bone destruction, which do not provide evi-

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Table 1. Clinical features of the current series of undifferentiated pleomorphic sarcoma of the sinonasal tract

No.	Sex/age (years)	Primary/ PIUPS	Primary tumor	Location	T stage	Treatment	Outcome
1	M/41	Primary		ES and MS	T2	S+RT	NED
2	F/58	Primary		MS	T2	S+RT	DOD
3	M/30	PIUPS	Olfactory neuroblastoma	ES	T1	S	NED
4	F/47	PIUPS	Undifferentiated carcinoma of the nasopharynx	Nasopharynx	T2	S+CT	DOD
5	F/49	PIUPS	SCC of MS	MS and NC	T2	RT	AWD

PIUPS: post-irradiated undifferentiated pleomorphic sarcoma, F: female, M: male, SCC: squamous cell carcinoma, MS: maxillary sinus, NC: nasal cavity, S: surgery, RT: radiation therapy, CT: chemotherapy, AWD: alive with disease, NED: no evidence of disease, DOD: dead of disease

Fig. 1. A bulky soft tissue mass in the right maxillary sinus with destruction of the maxillary walls and extension to the buccal space in gadolinium-enhanced T1-weighted MR image of primary UPS.

dent information for distinguishing squamous cell carcinoma nor lymphoma (Fig. 1). They were subjected to partial or total maxillectomy and postoperative adjuvant radiation therapy. One patient died of brain metastasis 17 months post-treatment because the tumor persisted despite total maxillectomy and radiation therapy, but the other patient remained alive with no evidence of disease 65 months post-treatment.

Three cases were post-irradiated UPS located within the radiation field for previous squamous cell carcinoma of the maxillary sinus, olfactory neuroblastoma, and undifferentiated carcinoma of the nasopharynx, respectively. The overall radiation doses were 59.4, 66.0, and 117.75 Gy, respectively. The time intervals between the radiation treatment and the diagnosis of UPS were 9.8, 3.2, and 3.1 years, respectively. The images similar to primary UPS did not show specific findings for the given diagnosis of UPS (Fig. 2). Immunohistochemistry revealed negative expression of desmin and cytokeratin, a finding that could exclude recurrent carcinoma (Fig. 3). Out of total three cases, the first patient (case 3) was treated initially by removing the tumors with endoscopic approach. However, local recurrence was found seventy-eight months after post-treatment and was successfully salvaged by same surgical endonasal approach with free resection margin. The second patient (case 4) had skull base invasion at diagnosis and was presented with severe nasal obstruction due to mass effect. Therefore, a debulking surgery following adjuvant chemotherapy was performed. Nevertheless, the patient died fourteen months after post-treatment due to uncontrolled local disease. The third patient (case 5) had poor general condition for surgery upon diagnosis and was treated with tomotherapy, a type of radiation therapy, and remained alive with the disease after 12 months.

DISCUSSION

UPS represents 25−40% of all soft tissue sarcomas in adults and may occur anywhere in the body, including the skin, deep soft tissues, and bone.[1] However, UPS involving the head and neck region is very rare, accounting for 3−10% of all cases. Among these cases, 30% occurs in the sinonasal tract, which is the most common location.[2]

The pathogenic factor most frequently implicated in UPS of the sinonasal tract is previous irradiation of the area.[4] After administration of 25−50-Gy radiation doses, post-irradiation sarcomas were reported to show a 0.06% risk with a mean of 15-year latency. Radiation doses greater than 50

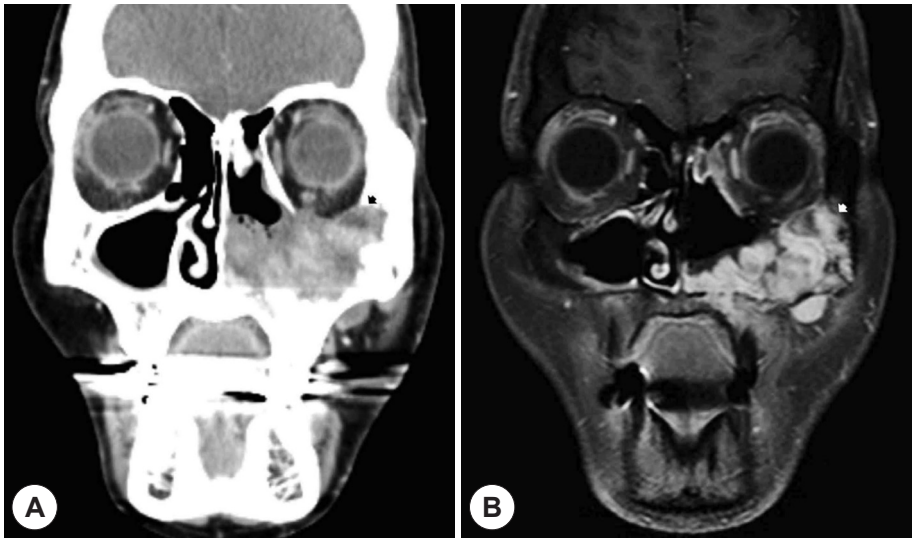

Fig. 2. Heterogeneously enhancing large mass with bony destruction of the maxillary walls and nasal cavity in CT scan (A) and MR image (B) of post-irradiated UPS.

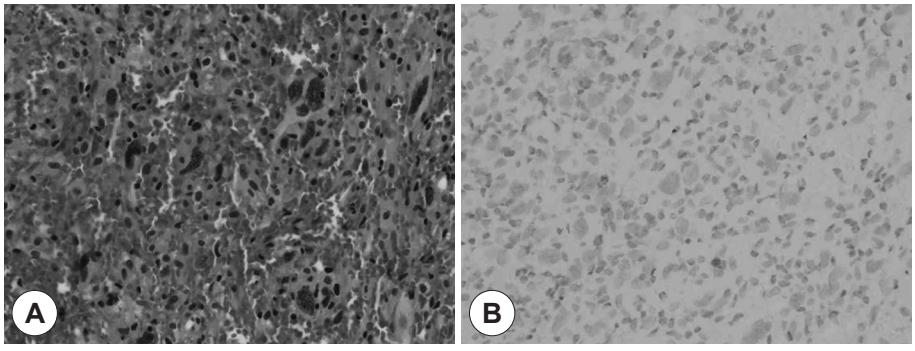

Fig. 3. Histopathology of radiation-induced undifferentiated pleomorphic sarcoma. The tumor consists of mixed spindle cells and roundedcells arranged in a storiform pattern. A: Hematoxylin-eosin (×400). B: Negative staining for cytokeratin by immunohistochemistry (×400).

Gy cause complete devitalization, and lower doses greater than 30 Gy are associated with permanent damage to the reparative mechanisms, leading to the development of secondary sarcoma.[5)6)] Our three patients with post-irradiated UPS had previously undergone radiation therapy with approximately more than 60 Gy. In addition, all of our post-irradiated UPS cases occurred within the radiation field, not at the edge of the radiation field. Post-irradiated UPS had occurred even approximately 10 years after the cure of squamous cell carcinoma of the maxillary sinus. Therefore, the patients with sinonasal malignancy should be observed closely after successful treatment with radiation therapy to identify radiation-induced secondary malignancies.

Pathological subtypes of UPS are storiform-pleomorphic, myxoid, inflammatory, and giant cell, and the storiform-pleomorphic type is the most common.[7)] All our patients were classified as storiform-pleomorphic type regardless of irradiation. The immunohistochemistry in the diagnosis of UPS plays an ancillary role.[7)] UPS usually shows focal reactivity for smooth muscle actin, but negative reactivity for desmin, h-caldesmon, S-100 protein, and epithelial markers.[7-9)] Positive immune-reactivity to vimentin, which has been used as a sarcoma marker, could also be helpful for the differential diagnosis of UPS from recurrent carcinoma.[10)11)] However, histiocytic markers (CD68, α1-antitrypsin, and α1-antichymotrypsin) has limited value in the diagnosis of UPS.[8)]

The previous studies reported that UPS was seen as a large aggressive mass with soft tissue invasion and bone destruction but had nonspecific attenuation, signal intensity, and enhancement on CT and MR images. Similarly, our cases showed a large soft tissue mass in the maxillary sinus with bone destruction on CT and/or MR images. Furthermore, there were no radiological differences between primary UPS and post-irradiated UPS. Thus, it is difficult to make a specific radiologic diagnosis.[15)]

Early, wide surgical excision with adequate margins is indicated because of the aggressive nature of the tumor.[2)12)16-18)] Because imaging findings of UPS are rather nonspecific,[3)] histopathological examination should precede the surgical

planning. Elective neck dissection is not necessary, because none of our cases or previously reported cases developed neck metastasis.[2)6)] Adjuvant radiotherapy is reported to improve local control but not to be associated with survival benefits. Although chemotherapy is considered in the patients with metastatic tumor, it remains controversial in UPS.[19)]

The prognosis of sinonasal UPS is poor, with 5-year overall survival rate between 20% and 50%.[2)12-14)] Wang *et al*. reported that age (≥50 years), previous radiation, and positive resection margin were significant adverse factors in the univariate analysis for 5-year overall survival. The prognosis of post-irradiated UPS with 5-year overall survival rate of 5.9% is worse than primary UPS with that of 71.4%.[4)] It may be very difficult to acquire adequate resection margins for post-irradiated UPS because intraoperative assessment of the tumor margin is difficult in an irradiated field.[4)] In addition, re-irradiation is not feasible for preventing the recurrence of UPS. The local recurrence of UPS and distant metastasis to lung, bone, and brain frequently occur, while regional metastases are rare.[11)12)]

In our post-irradiated UPS cases, only T1 tumors localized in the ethmoid sinus that did not invade the orbit were cured after resection via an endonasal endoscopic approach. However, T2 primary UPS in the ethmoid and maxillary sinuses was treated successfully using maxillectomy and adjuvant radiation therapy despite destruction of the maxillary sinus wall. Similar to our findings, a multicenter study reported that stage I or II is included in the independent favorable prognostic factors with respect to disease-specific survival in primary UPS.[20)]

CONCLUSION

UPS of the sinonasal tract is rare. Among our cases, although only five were reported, the radiological findings were not specific for UPS whether they were primary or post-irradiated. Furthermore, post-irradiated sinonasal UPS showed high rates of remnant disease after treatment. Conversely, primary sinonasal UPS may achieve an acceptable outcome if the tumor is resected aggressively with adequate surgical margins and adjuvant radiotherapy.

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