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Clinical Presentation and Management of Patients with Bone Metastases (BMet) from Neuroendocrine Tumors (NETs): Pooled Results from Two Institutional Databases

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Background: NETs metastasize to bone; however, a multi-institution evaluation of the incidence and complications of BMet across multiple NET subtypes has not previously been conducted.

Methods: We identified patients with BMet from two institutional databases of patients who presented to OSU or UCSF with a diagnosis of NET between 2004-2008. BMet incidence, occurrence of skeletal-related events (SREs), and interventions were analyzed by using summary statistics and categorical methods. Time-to-event data were assessed by Kaplan-Meier estimates and log-rank tests.

Results: Between 2004-2008, 82 of 697 NET patients (11.8%) at OSU or UCSF were reported to have BMet. Of these, most were low or intermediate grade: 29 (35%) had carcinoid; 24 (29%) had pheochromocytoma or paraganglioma; 14 (17%) had pancreatic NET (PNET); and 11 (16%) had a high-grade NET. 56% were men, and mean age was 50.1. At time of BMet diagnosis, 60% were symptomatic. BMet occurred 23% of pheochromocytomas and paragangliomas (24 of 152), 23% of high-grade NETs (11 of 46), 9% of carcinoids (29 of 309), and 9% of PNETs (14 of 152). SREs according to tumor subtype are described in Table 1. 60 (80.5%) patients with BMet received treatment: 51% received radiation, 46% received a bisphosphonate, 17% underwent surgery, 12% received ^{131}I-MIBG, and 5% received denosumab. 46% were treated with >1 treatment modality. Among patients in whom BMet were not present at time of NET diagnosis, median time to development of BMet was 13.5 months. Median overall survival among patients with BMet was 45.3 months.

Conclusion: Among patients with NET, and particularly among high-grade NET, pheochromocytoma and paraganglioma subtypes, clinicians should be vigilant regarding the risk of developing BMet and associated complications. For patients who develop BMet, SREs are common and preventive therapy with a bisphosphonate or denosumab may be of value given extended survival of NET patients.

Table 1. Description of SREs among all patients diagnosed with BMet.

	Carcinoid (N=29)		PNET (n=14)		High-grade NET (n=11)		Pheo/para† (n=24)		Other* (n=4)		TOTAL (n=82)	
	N	%	N	%	N	%	N	%	N	%	N	%
Bone pain	19	65.5	10	71.4	6	54	15	62.5	2	50	52	63.4
Cord compression	1	3.4	1	7.1	1	10	5	20.8	0	0	8	9.8
Pathologic fracture	2	6.9	1	7.1	2	20	2	8.3	1	25	8	9.8
Hypercalcemia	0	0	0	2	1	10	2	8.3	0	0	3	3.7
Surgery or XRT‡	14	48.3	8	57.1	3	50	11	45.8	2	60	38	46.3

† Pheochromocytoma or paraganglioma

* Other = adrenocortical carcinomas and atypical carcinoid tumors

‡ Surgery or radiation delivered to a symptomatic BMet