

Additional value of immunohistochemistry to 68Ga-DOTATOC scan in tumor induced osteomalacia

¹연세대학교 의과대학 내과학교실, ²연세대학교 의과대학 병리학교실

*이승현¹, 이유미¹, 홍남기¹, 김상겸²

Background/Aims: Tumor induced osteomalacia(TIO) is a rare paraneoplastic syndrome caused by oversecretion of fibroblast growth factor 23(FGF23) secreted by mesenchymal tumors. Locating the tumor is critical, as complete removal is curative. Suspicious lesions are confirmed by anatomical imaging, and if needed, selective venous sampling with measurement of FGF23. However, there is a possibility of false positive results, so histological confirmation or additional diagnostic method might be necessary. Demonstration of FGF23 by immunohistochemistry(IHC) or RT-PCR has been used to confirm the diagnosis of TIO. But FGF23 is not usually available in diagnostic pathology laboratories. Also, FGF23 expression by IHC is frequently focal, so it limits diagnostic utility, particularly in a small biopsy. On the other hand, since 68Ga-DOTATOC scan which has been recommended as a first line modality for localizing TIO has a higher affinity for somatostatin receptor 2A(SSTR2A), IHC for SSTR2A might be helpful in confirming TIO. Therefore, we investigated the association between FGF23, SSTR2A IHC and 68Ga-DOTATOC scan. **Methods:** We retrospectively analysed the data of patients referred from November 2010 to December 2018 in Severance hospital. 9 patients(4 males and 5 females) with suspected TIO underwent IHC for FGF23 and SSTR2A. Eight of them underwent 68Ga-DOTATOC scan. FGF23, SSTR2-expression were scored by pathologists. We defined as follows ; Total histologic score (H-score) = percentage score(0,1,2) * intensity score(1,2,3) **Results:** FGF23 was stained focally, and showed non-specific, various expressions from nucleus to cytoplasm. In contrast, SSTR2A staining was present in the great majority of tumor cells, and uniformly expressed in cytoplasm. There was a significant difference in the expression of the two antibodies by the T-test. SSTR2 expression was significantly better than FGF23 expression.($p=0.0294$) 68Ga-DOTATOC scan was performed in 8 cases and all cases were positive. **Conclusions:** IHC for SSTR2A is highly sensitive for the diagnosis of TIO. And SSTR2-IHC correlates with 68Ga-DOTATOC scan. It might be helpful to confirm TIO when there is a suspicion of equivocal interpretation in the 68Ga-DOTATOC scan.

Table 1. Patient characteristics

Patient	Age (yr)	Gender	Symptom	Duration (mo)	P(mg/dL) 2.5-4.1	Calcitriol (ng/mL) 20-80	PTH (pg/mL) 15-65	ALP	TRP 0.85-0.95	FGF23 (ng/mL) 10-50	DXA value
1	60	F	back pain	28	1.9	15.8	23.7	176	35.4	-	-3.7
2	24	M	multiple pain, height loss	31	1.8	42.6	52.9	234	85.3	699.5	-
3	26	F	back pain, knee pain	40	2.1	97.2	220.2	203	63	156	-1.7
4	31	F	back pain	12	1.4	-	88.1	239	-	159.04	-2.5
5	37	F	multiple joint pain	12	1.7	14.8	95.4	209	68.6	335.08	-
6	51	M	Both hip Fx	13	1.3	-	80.8	192	77.9	210.65	-2.1
7	53	M	multiple pain, height loss	24	2.4	97.1	46.4	356	80.1	163.88	-2.2
8	59	F	chest pain	36	2	-	105.1	168	78	182.72	-2.5
9	60	M	Rib pain, height loss	48	2.5	-	98.4	451	65	252.14	0.8

Yr, years; mo, months; P, phosphorus; PTH, parathyroid hormone; TRP, tubular reabsorption of phosphate; FGF23, fibroblast growth factor 23; DXA, dual-energy x ray absorptiometry; F, female; M, male

Table 2. Immunohistochemistry and ⁶⁸Ga-DOTATOC scan

Patient	Cytologic grade	GCT-like feature	Rich vasculature	Other	FGF23	H-score	SSTR2	H-score	⁶⁸ Ga-DOTATOC	Whole body sampling
1	1	0	0	Short spindle to epithelioid	DS:C	6	DS:C	6	Never done	Never done
2	0	0	1	Fibrosis like	DM:C	4	DS:C	6	Positive	Negative (1.06)
3	0	0	0	Fibrosis like	FM:C	2	DS:C	6	Positive	Positive (6.62)
4	0	0	0	Fibrosis like	FW:C	1	DS:C	6	Positive	Negative (1.2)
5	0	0	0	Fibrosis like	FM:C	2	DS:C	6	Positive	Negative (0.97)
6	1	1	1	SFT like	DS:N	6	DS:C	6	Positive	Negative (1.42)
7	0	1	0		DS:N	6	DS:C	6	Positive	Positive (2.74)
8	0	1	0	GCT like	DM:N	4	DS:C	6	Positive	Never done
9	0	0	1	SFT like	DS:N	6	DS:C	6	Positive	Positive (1.67)

⁶⁸Ga, ⁶⁸Gallium; GCT, giant cell tumor; SFT, solitary fibrous tumor; FGF23, fibroblast growth factor 23; H-score, total histologic score (=percentage score(0,1,2) * intensity score(1,2,3)); SSTR, somatostatin receptors; D, diffuse; F, focal; S, strong; M, moderate; W, weak; C, cytoplasmic; N, nuclear