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Case Report

# Giant parathyroid adenoma and hungry bone syndrome in MEN1 syndrome: A case report ☆

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ABSTRACT

An 18-year-old male with multiple endocrine neoplasm type 1 (MEN1) syndrome presented with hyperparathyroidism. Parathyroidectomy was performed. Patient complained of bone pain afterwards, multiple imaging modalities revealed features of osteitis fibrosa cystica and biochemical profile showed features of hungry bone syndrome. Incidental suspicious pancreatic lesion was initially revealed by $^{18}$F-FDG PET/CT scan while MRI further characterized the possibility of insulinoma. Ultimately, the patient was diagnosed of MEN1 syndrome by genetic test. This case report demonstrates the utilization of various imaging modalities such as ultrasound, $Tc^{99m}$-sestamibi parathyroid scintigraphy, bone scintigraphy, CT, PET/CT and MRI, which leads to ultimately the diagnosis of MEN1 syndrome.



## Background

Giant parathyroid adenoma is an uncommon condition characterized by the abnormal enlargement of the parathyroid gland, resulting in excessive production of parathyroid hormone (PTH) [1]. Definite treatment of severe primary hyperparathyroidism (PHTH) is surgical removal of the parathyroid adenoma. Localization and characterization of the lesion are often aided by radiological investigations, namely ultrasound and $Tc^{99m}$-sestamibi parathyroid scintigraphy [2]. This case highlights the importance of radiological assessments including the identification of the tumor, evaluation of its characteristics, and assessment of potential skeletal involvement in a patient with giant parathyroid adenoma and complicated by hungry bone syndrome (HBS) post-operatively, which leads to ultimately the diagnosis of MEN1 syndrome.

## Case presentation

An 18-year-old Asian male initially presented with primary hyperparathyroidism with parathyroid hormone up to 335.4 pmol/L (normal range: 2.3-9.3) and severe hypercalcemia with calcium up to 4.11 mmol/L (normal range: 2.10-2.57) without significant improvement despite use of bisphosphonate, hyperhydration and calcitonin [3]. He was referred for ultrasound

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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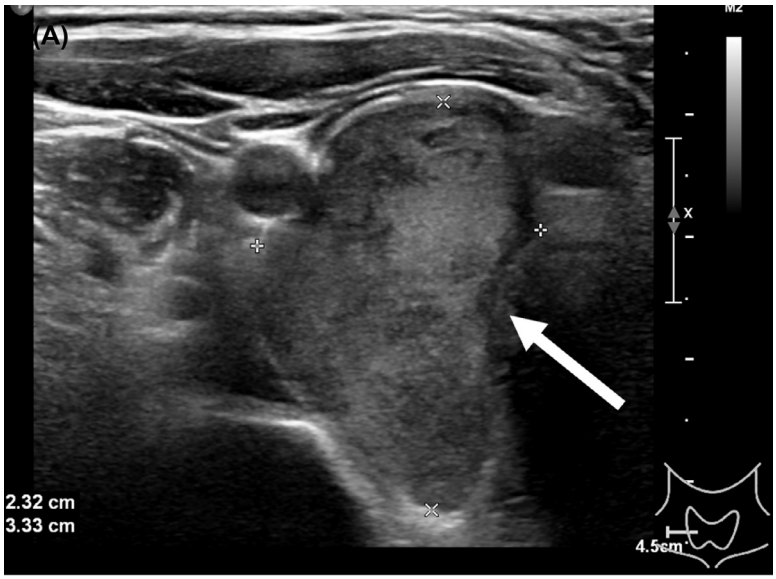


**Fig. 1 – (A) Ultrasound imaging revealed large heterogeneous hypoechoic nodule in the expected right parathyroid gland.**

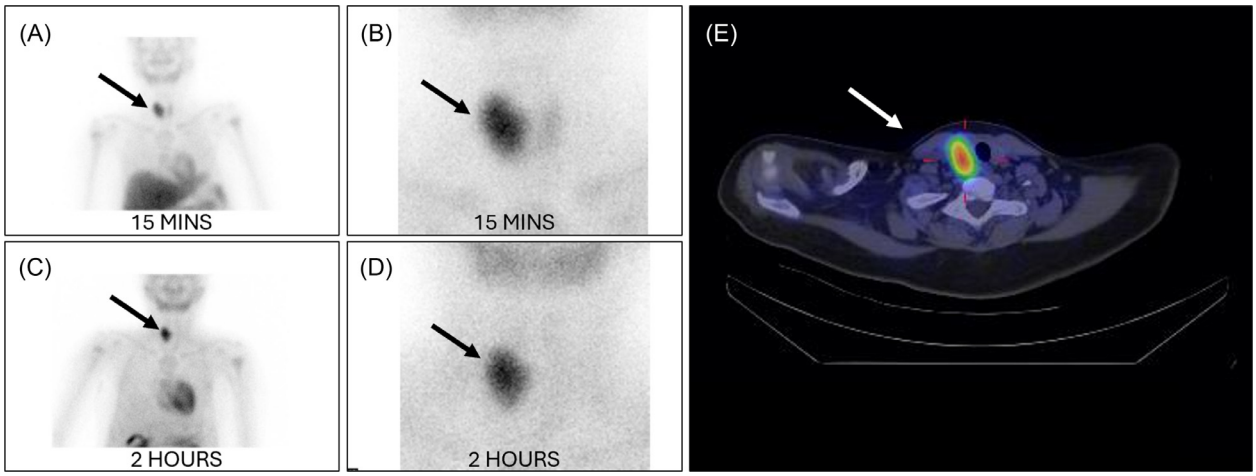


**Fig. 2 – Parathyroid scintigraphy revealed (A and B) intense increased uptake in early planar images (15 minutes) with (C and D) differential washout over right thyroid lobe in delayed planar images (2 hours). (D) $Tc^{99m}$-sestamibi SPECT/CT fusion trans-axial image showed hypodense nodular mass (arrows) posterior to right thyroid lobe, there is no other focal increased uptake in rest of the neck nor mediastinum.**

neck and $Tc^{99m}$-sestamibi parathyroid scintigraphy. Ultrasound imaging revealed large heterogeneous hypoechoic nodule in the expected right parathyroid gland (Fig. 1). Parathyroid scintigraphy, performed at our center, revealed intense increased uptake with differential washout in right thyroid bed region, SPECT/CT showed hypodense nodular mass posterior to right thyroid lobe, there is no other focal increased uptake in rest of the neck nor mediastinum (Fig. 2). Parathyroidectomy was performed with intraoperative finding of a large 3.5 cm right parathyroid adenoma abutting right upper pole of thyroid. Histological examination confirmed giant parathyroid adenoma as the tumor weight more than 2 g (10.27 g).

Two weeks later, patient complained of bone pain over right arm and both thighs during follow up. X-ray of skeletal survey, CT and MRI of extremities and hip were performed, with the findings of multiple lytic bone lesions, right humeral fracture, and bilateral femoral fractures (Fig. 3). Pathological fractures were suspected. Biochemical profile showed the patient had a hypocalcemia level of 2.01 mmol/L (normal range: 2.10-2.57), hypophosphatemia level of 0.4 mmol/L (normal range: 0.8-1.6), hypomagnesemia level of 0.59 mmol/L (normal range: 0.70-0.91). elevated alkaline phosphatase level of 1784 IU/L (normal range: 52-171) and low 1,25-dihydroxyvitamin D level of 12 nmol/mL (normal range: 50-220). A diagnosis of hungry bone syndrome was made in view of post-parathyroidectomy state, imaging findings, and biochemical profile.

Subsequent bone scintigraphy was arranged for further evaluation of skeletal involvements showing diffuse markedly

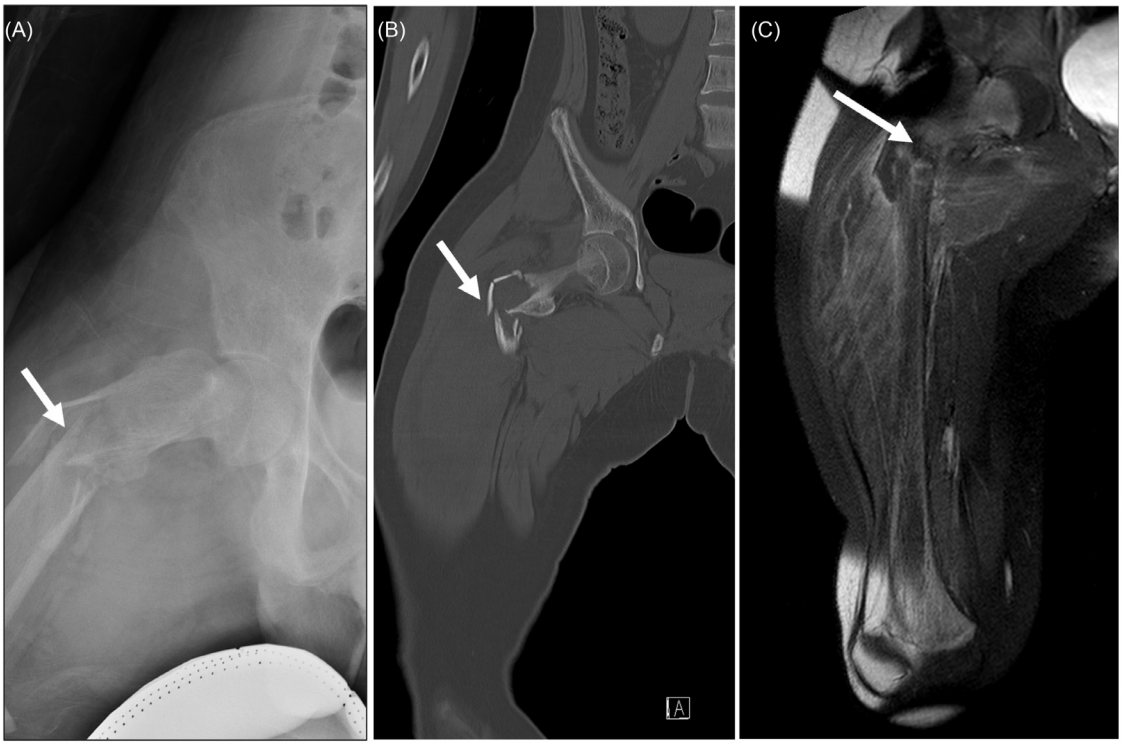


**Fig. 3 – Right femoral fracture (arrows), (A) X-ray, (B) coronal CT, and (C) coronal MRI T2 weighted.**

increased tracer uptake in axial and appendicular skeletons and features of right femoral fracture (Figs. 4A and B). $^{18}$F-FDG PET/CT was done for exclusion of primary malignancy including Langerhans cell histiocytosis as well as bone metastases. Similar osseous findings were seen in $^{18}$F-FDG PET/CT (Fig. 4C) with presence of osteitis fibrosa cystica and additional mild FDG avidity in pancreas (Fig. 5) [4]. Otherwise, no suspicious FDG-avid primary malignancy was detected by the $^{18}$F-FDG PET/CT scan. Blood test revealed elevated prolactin of 501 mIU/L (normal range: 57-322). MRI showed a 1 cm T1-hypointense T2 hyperintense lesion with restricted diffusion in pancreatic body (Fig. 5) and suspicious of insulinoma while assessment of pituitary was unremarkable. Multiple endocrine neoplasm type 1 (MEN1) was suspected, and genetic test confirmed the diagnosis. The use of FDG PET/CT showed incidental finding of focal mild FDG-avidity in pancreas, which led to subsequent MRI assessment of pituitary gland and genetic test for MEN1 syndrome [5].

## Discussion

Giant parathyroid adenoma refers to an unusually large tumor of the parathyroid gland, typically exceeding 2-3 grams in weight. The regulations of calcium and phosphorus can be disrupted due to high level of PTH production, leading to hypercalcemia and subsequent complications.

The pathophysiology of giant parathyroid adenoma involves the autonomous production of PTH, which results in hypercalcemia. The excessive PTH stimulates the release of calcium from bones, leading to bone resorption and weakening of the skeletal structure. Additionally, hypercalcemia can cause increased renal calcium reabsorption, leading to the formation of kidney stones. Patients with giant parathyroid adenoma may present with symptoms such as fatigue, bone pain, kidney stones, and neuropsychiatric disturbances.

Hungry bone syndrome is a phenomenon observed following parathyroidectomy, manifests as sudden drop in PTH levels [6], leading to a surge in bone formation. This results in the rapid and extensive deposition of calcium into the bones, causing a state of severe hypocalcemia known as hungry bone syndrome [7].

The mechanism behind hungry bone syndrome involves the restoration of the calcium balance in the body. As PTH levels decrease after surgery, bone formation accelerates to compensate for the increased calcium uptake that occurred during the hyperparathyroidism state. This phenomenon can result in severe hypocalcemia, muscle cramps, tetany, and even cardiac arrhythmias. Treatment of hungry bone syndrome includes calcium and vitamin D supplementation to promote bone healing and prevent further complications [8].

For our patient, giant parathyroid adenoma was histologically confirmed while the small pancreatic lesion was a suspicious radiological finding without histological evaluation. No suspicious lesion was detected in the pituitary gland. The clinical diagnosis of MEN1 syndrome can be made with occurrence of 2 or more primary MEN1 tumor types in parathyroid gland, anterior pituitary, and enteropancreatic regions and the confirmation of MEN1 mutation is made by genetic testing [9]. Therefore, our patient fulfilled the clinical diagnostic criteria

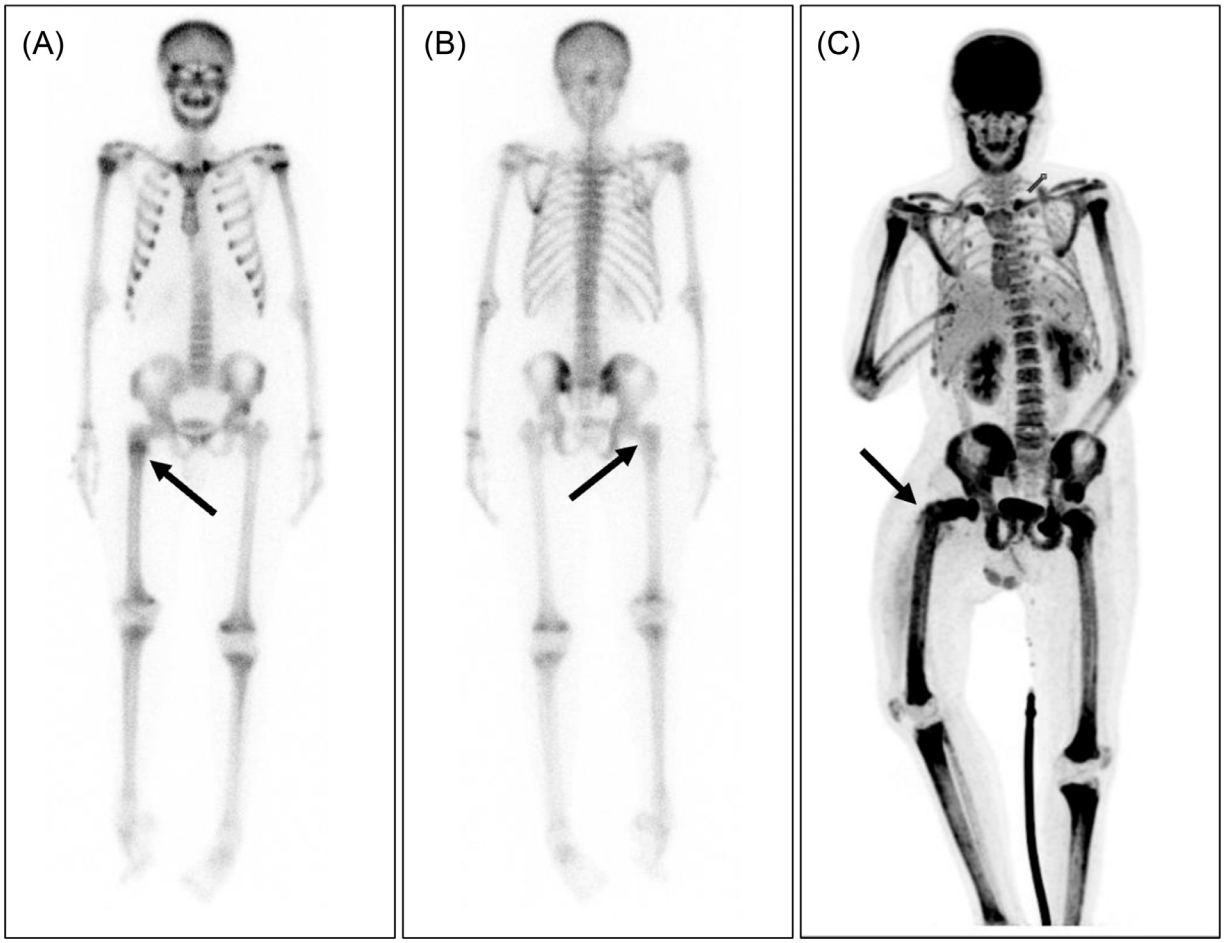


**Fig. 4 – Bone scintigraphy shows diffuse markedly increased tracer uptake throughout whole body skeleton, involving skull, mandible, sternum, costochondral joints, vertebral column, bony pelvis, periarticular region of long bones with reduced urinary tracer accumulation and increased bone-to-soft-tissue contrast. Patchy markedly increased uptake at inferior angle of left scapula, right neck of humerus, bilateral sacroiliac joints, left anterosuperior iliac spine, left acetabulum and right proximal femur (arrows), consistent with known pathological fractures. (A) Anterior whole body planar image of bone scan, (B) posterior whole body planar image of bone scan, (C) maximal intensity projection of $^{18}$F-FDG PET/CT shows similar patchy hypermetabolic bone uptake pattern.**

of MEN1 syndrome. Furthermore, MEN1 mutation was positive in our patient.

Radiological investigation plays a pivotal role in the diagnosis and management of giant parathyroid adenoma, as well as the assessment of hungry bone syndrome. Various imaging techniques are employed to locate and visualize the parathyroid adenoma, evaluate its characteristics, and assess skeletal involvement.

Ultrasound is a commonly used imaging modality to identify parathyroid adenomas. It can provide real-time images of the neck, allowing for the detection of abnormal masses in the region of the parathyroid glands. Ultrasound can also help differentiate between parathyroid adenomas and other neck masses or thyroid nodules. The ultrasound imaging of the giant parathyroid adenoma in this patient showed a large heterogeneous hypoechoic nodule in the expected right parathyroid gland, with corresponding intense increased uptake and differential washout over right thyroid lobe in $Tc^{99m}$-sestamibi parathyroid scintigraphy.

$Tc^{99m}$-sestamibi parathyroid scintigraphy is another valuable tool in the localization of parathyroid adenomas. The scan helps identify the precise location of the adenoma, making minimal invasive surgery possible [10]. It can also be particularly useful in cases with ectopic hyperfunctioning parathyroid tissue or when ultrasound is inconclusive. New imaging modalities are emerging for the localization of parathyroid adenoma [11].

The corresponding mild FDG-avid pancreatic body lesion in $^{18}$F-FDG PET/CT scan showed T1-hypointense T2 hyperintense with restricted diffusion in subsequent MRI, raising the suspicion of insulinoma and eventually leading to genetic test for confirmation of MEN1 syndrome.

Radiological investigations are also crucial in assessing the skeletal involvement associated with hyperparathyroidism and hungry bone syndrome. Radiographs, CT, and bone scintigraphy can be employed to evaluate the presence of osteopenia, osteoporosis, fractures, or other skeletal abnormalities like osteitis fibrosa cystica associ-

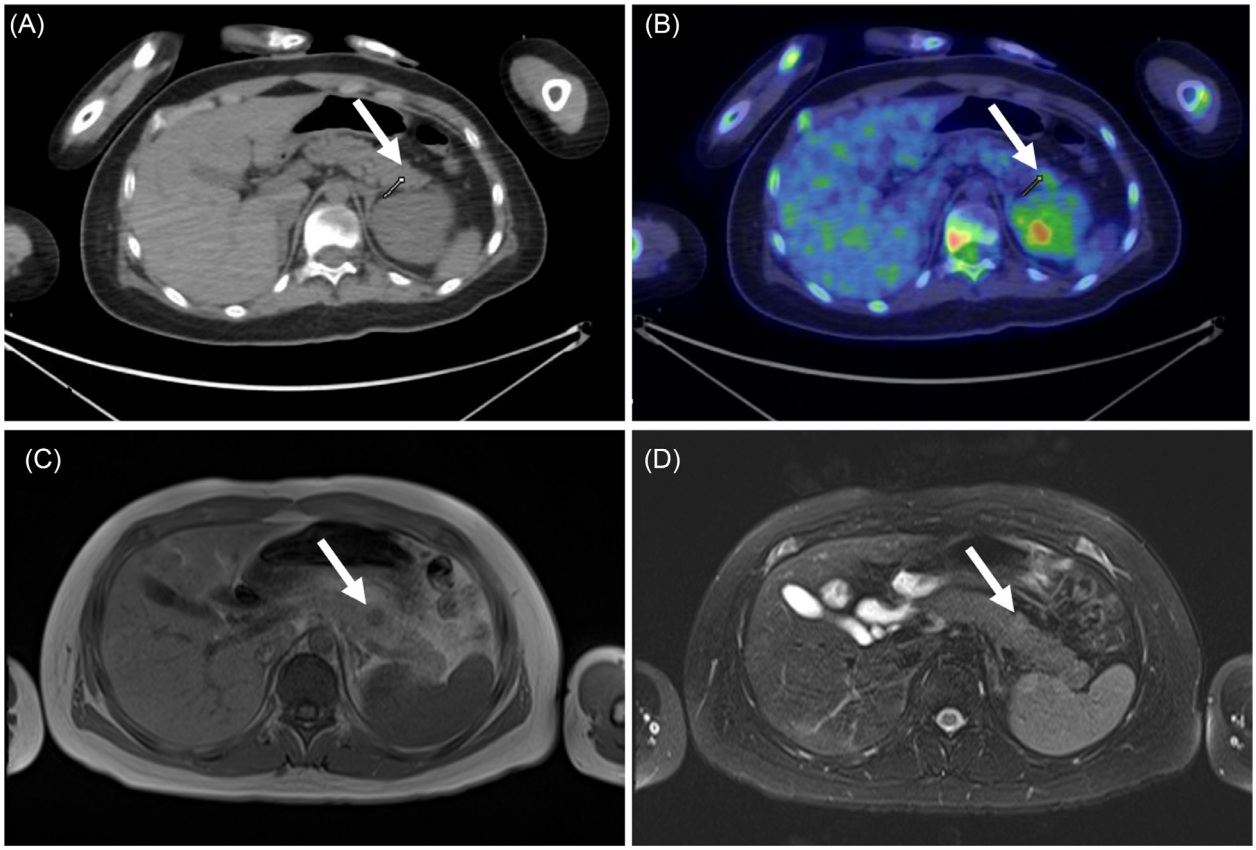


**Fig. 5 – Incidental finding of mild FDG avidity in pancreas, (A) CT only trans-axial image, (B) $^{18}$F-FDG PET/CT fusion trans-axial image. MRI showed a 1 cm (C) T1-hypointense (D) T2 hyperintense lesion with restricted diffusion in pancreatic body and suspicious of insulinoma.**

ated with hyperparathyroidism and hungry bone syndrome [12–13].

## Conclusion

Giant parathyroid adenoma with hungry bone syndrome is a complex condition that requires a comprehensive approach for diagnosis and management. Radiological investigation plays a crucial role in the accurate identification of the adenoma, evaluation of its characteristics, and assessment of skeletal involvement. This information is vital for surgical planning, optimizing patient outcomes, and minimizing the risk of complications. This case report demonstrates the utilization of various imaging modalities such as ultrasound, $Tc^{99m}$-sestamibi parathyroid scintigraphy, bone scintigraphy, CT, PET/CT and MRI, which leads to ultimately the diagnosis of MEN1 syndrome by genetic test.

## Ethical approval

The study was approved by the Central Institutional Review Board of Hospital Authority, Hong Kong (Ref No.: CIRB-2024-025-4). This study was performed in line with the principles of the Declaration of Helsinki. The patient was provided informed consent for the publication of this case report.

## Patient consent

Informed consent of the patient was obtained.

## Authors' Contributions

Lau Jeremy Hugh Yen-hey designed the study, acquired, and analyzed the data and drafted the manuscript. Ng Koon Kiu, Wong Wai Chung and Kung Boom Ting critically revised the manuscript for important intellectual content. Lau Jeremy Hugh Yen-hey, Ng Koon Kiu, Wong Wai Chung and Kung Boom Ting had full access to the data, contributed to the study, approved the final version for publication and take responsibility for its accuracy and integrity.

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