# **Case Report**

# Pulmonary Embolism and Subclavian Vein Thrombosis in a Patient with Parathyroid Carcinoma: Case Report and Review of Literature

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Parathyroid carcinoma is a rare etiology of primary hyperparathyroidism responsible for 0.4 to 5.2% of all primary hyperparathyroidism cases. The overt hyperparathyroid bone or renal disease with palpable neck mass, as well as severe hypercalcemia with extremely high parathyroid hormone, are clinical parameters raising the suspicion for parathyroid carcinoma. However, a definite diagnosis can be confirmed only by examining the histopathology of the tumor. The curative treatment solely depends on an en bloc surgical approach. Therefore, preoperative clinical diagnosis of carcinoma is essential for optimal surgical planning. The present study reported asymptomatic subclavian vein thrombosis and pulmonary embolism in parathyroid carcinoma, suggesting paraneoplastic syndrome of hypercoagulability in this cancer type. The presence of this paraneoplastic syndrome in a case of overt clinical hyperparathyroidism in addition to a palpable neck mass indicated the diagnosis of carcinoma preoperatively in the present patient, which led to an en bloc surgical plan. Since this paraneoplastic syndrome can be asymptomatic, the exploration of this syndrome by a commonly used imaging technique for parathyroid tumor localization, computerized tomography, would enable a preoperative diagnosis of cancer, especially in an equivocal situation.

Keywords: Parathyroid carcinoma, Pulmonary embolism, Venous thromboembolism, Paraneoplastic syndrome, Hypercalcemia

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Among the malignant endocrine neoplasms, parathyroid carcinoma is the rarest form and is responsible for only 0.2 to 0.5% of all malignant endocrine tumors. It is a slow-growing tumor frequently occurring in the fifth decade, which is approximately 10 years earlier than patients who suffer with parathyroid adenoma<sup>(1)</sup>. Parathyroid carcinoma usually presents with a clinical syndrome of primary hyperparathyroidism; however, it accounts for only 0.4 to 5.2% of all reported cases of primary hyperparathyroidism<sup>(2,3)</sup>. Although there is no clinical parameter for definite diagnosis of parathyroid carcinoma, some clinical parameters should raise suspicion for this carcinoma, including acute and severe symptoms of hypercalcemia in combination with the presence of overt bone disease and renal stone disease, palpable neck mass that is adherent to the adjacent structure, recurrent laryngeal nerve palsy or

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local neck pain, extremely high levels of calcium and parathyroid hormone, and the presence of familial syndromes associated with parathyroid carcinoma or distant metastases<sup>(4)</sup>. Owing to the unreliability of these clinical parameters, parathyroid carcinoma is considered a diagnostic dilemma<sup>(5)</sup>. Although clinical suspicion of this cancer alone is insufficient to make a definite diagnosis, the clinical suspicions of malignant disease would guide clinicians to choose an appropriate imaging technique for tumor localization to inform a surgical approach, which is currently the only definite treatment for this parathyroid carcinoma.

Hypercoagulability is a common paraneoplastic syndrome of malignant diseases, in particular, relating to carcinoma of the prostate, colon, lung, breast, and ovary<sup>(6)</sup>. This paraneoplastic syndrome usually manifests itself with occurrence of deep vein thrombosis and pulmonary embolism. Malignant diseases have a 4.1 fold increased risk of thrombosis, especially in patients with advanced diseases and receiving chemotherapy treatment<sup>(7)</sup>. The present case report described a patient with parathyroid carcinoma who presented with overt osteitis fibrosa cystica and nephrocalcinosis, as well as asymptomatic pulmonary

embolism. The results of a MEDLINE search using the keywords of either "parathyroid carcinoma and thromboembolism" or "parathyroid carcinoma and hypercoagulation", revealed only one case with venous thromboembolism that had been previously described in a patient with parathyroid carcinoma<sup>(8)</sup>. Thus, in the present report, we demonstrated that the paraneoplastic syndrome of asymptomatic thromboembolism was one of the rare manifestations of parathyroid carcinoma and was a helpful clue for the diagnosis of parathyroid carcinoma. We also provided evidence suggested that the computerized tomography, which could reveal the asymptomatic thromboembolism, was a useful tool for diagnosis of parathyroid carcinoma preoperatively and then for planning a curative surgery. The present case report had been approved by the Ethics Committee of the Faculty of Medicine, Chiang Mai University.

#### **Case Report**

A 54-year-old Thai man had a painful tumorlike lesion at his left wrist for six months. Simultaneously, he also reported constipation and polyuria, which were symptoms with a high correlation to hypercalcemia. He never had hematuria, passing stones, back pain, or decreased in height. He did not report any neck mass, and had no symptoms that correlated to neck mass, including pain, dysphagia, or hoarseness. A thorough review of his medical history revealed no occasions of edema of any extremities, chest pain, or dyspnea. On physical examination, a firm and fixed mass was detected at his left lower cervical region, measuring approximately 5x6 cm in size. Multiple tumor-like lesions were found throughout his body, including left wrist, right hand, right proximal arm and both sides of the anterior chest wall. Laboratory investigation showed an extremely high level of serum calcium and intact parathyroid hormone (iPTH; 17.1 mg/dL and 2,253 pg/mL, respectively), indicating primary hyperparathyroidism in this patient. Other laboratory investigation showed a mildly elevated serum creatinine level of 1.6 mg/dL with an eGFR of 48.1 mL/min/1.73 m<sup>2</sup> (by MDRD), indicating chronic kidney disease stage 3. Afterward, bilateral nephrocalcinosis was demonstrated by renal ultrasound. The skeletal radiographic study showed subperiosteal bone resorption of the phalanges, as well as salt and pepper appearance of the skull, consistent with osteitisfibrosacystica. In addition, discrete expansile cystic lesions were detected in multiple bony sites, consistent with the tumor-like lesions found on physical examination. In addition, a pathological

fracture was demonstrated through the cystic bony lesion in the right proximal humerus.

Because of the overt presentation of primary hyperparathyroidism and palpable neck mass, parathyroid carcinoma was suspected. The 99mTc methoxy isobutyl isonitrile (MIBI) were carried out and demonstrated a huge, oval-shaped lesion showing heterogenous radiotracer uptake occupying the left thyroid bed that persisted in the late image, suggesting a parathyroid gland tumor. Simultaneously, this 99mTc scintigraphy also illustrated multiple radiotracer uptake within the skeleton, consistent with the expansile cystic lesions in the plain skeletal radiography. Because parathyroid carcinoma is suspected in this case, these painful skeletal lesions could possibly be skeletal metastases, in particular due to the positive radiotracer uptake in the 99mTc MIBI scintigraphy. A skeletal biopsy was performed at the left wrist lesion and pathological investigation finally confirmed the diagnosis of a brown tumor. Awaiting further management, zoledronic acid was administered to lower serum calcium levels and to halt further development of bone lesions.

Without the evidence of metastases, curative surgery was planned. Next, computerized tomography (CT) of the neck and chest were carried out to determine the boundaries of the tumor. The CT of the neck demonstrated a well-defined oval shape heterogenous hypodense lesion with internal necrosis and intense enhancement at the left paratracheal region in the posterolateral to left lobe of the thyroid gland, measuring 4.7x5.7x7.7 cm in transverse, anteroposterior (AP), and vertical diameters, respectively (Fig. 1). There was no significant cervical lymphadenopathy. The CT of the chest did not show either mediastinal or pulmonary mass. Surprisingly, incidental findings of intraluminal filling defects in the right subclavian vein and lower segment branch of the left pulmonary artery, indicated right subclavian vein thrombosis and left pulmonary artery embolism, respectively (Fig. 2). Due to the possibility of venous thromboembolism, low molecular weight heparin was promptly initiated and then stopped 24 hours before surgery.

Finally, en bloc surgery was scheduled. A 8x5 cm firm, dark brown, left parathyroid lobulated mass with an irregular surface and multiple cystic component was intraoperatively identified. In addition, a 0.5 cm nodule in the thyroid isthmus and two 1-cm lymph nodes in the neck level VI were found. The parathyroid mass, left lobe and isthmus of the thyroid, and the identified lymph nodes were totally removed



Fig. 1 A computerized tomography of the neck revealing a well-defined oval shaped heterogenous hypodense lesion with intense enhancement at the left paratracheal region posterolateral to the left lobe of the thyroid gland, measuring 4.7x5.7x7.7 cm transversely, AP, and vertical diameters respectively (white arrow). There was internal necrosis in this mass. There was no significant cervical lymphadenopathy.

in an en bloc manner with the adjacent soft tissue. The iPTH and calcium level of the patient progressively declined after the operation. The iPTH and calcium level went down from 2,852 pg/mL and 15 mg/dL at a day before operation to 103.3 pg/mL and 13.9 mg/dL on the first day after surgery and then to 11.19 pg/mL and 9.1 mg/dL on the second day following the operation. Oral calcium and calcitriol were initiated on the second day postoperation; however, the patient experienced asymptomatic hypocalcemia of 6.8 mg/dL on the third day after surgery. On the third day postoperative, incomplete weakness and numbness of both lower extremities without bowel and bladder dysfunction were recognized. A gadolinium-enhanced magnetic resonance imaging (MRI) of the spine was carried out and showed expansile bony lesions within the posterior elements of the fifth and sixth thoracic spine, causing moderate spinal cord compression. Because of the normalized level of parathyroid hormone, osteitis fibrosa cystica of the spine was suspected. The neurological symptoms of the patient were improved with non-surgical treatment, including intravenous dexamethasone. Finally, the patient was discharged with oral calcium and calcitriol for hungry bone syndrome, warfarin to treat the venous thromboembolism, as well as an external cast for the fracture of the right humerus. The pathological examination of the removed parathyroid tumor demonstrated parathyroid neoplasm with capsular and





vascular invasion, confirming parathyroid carcinoma (Fig. 3A, B). However, the removed thyroid and lymph nodes did not indicate cancer involvement. Three months after surgery, the MRI of the spine was repeated and illustrated an improvement of the brown tumor in the thoracic spine and ribs. Radiography of the right humerus also showed a decrease in size of the brown tumor and an appearing of callus formation at the fracture site. On the contrary, the iPTH increased up to 121.8 pg/mL when the serum calcium was at 8.2 mg/dL. The 99mTc MIBI scintigraphy was then repeated and no radiotracer uptake was shown. Thereafter, his iPTH and serum calcium were regularly followed up and were shown to be within normal range. The iPTH and serum calcium were 32.3 pg/mL and 10.2 mg/dL at the 9th month, as well as 49.2 pg/mL



Fig. 3 (A) A pathological examination showed uniform cells with minimal atypia arranged in trabecular patterns with fibrous bands, suggesting parathyroid neoplasm (H&E, 40x). (B) A pathological examination demonstrated parathyroid capsular invasion, confirming parathyroid carcinoma. There was no lymphovascular space invasion (H&E, 40x).

and 9.4 mg/dL at the 13th month after surgery. The diagnosis and treatment algorithm of the present patient were illustrated in chronological order (Fig. 4).

#### **Discussion and Review of literature**

In the present report, the authors had demonstrated a patient with parathyroid carcinoma who presented with severe hypercalcemia, nephrocalcinosis and overt hyperparathyroid bone disease in a concomitance with asymptomatic pulmonary embolism and subclavian vein thrombosis, which was a paraneoplastic syndrome rarely reported in parathyroid carcinoma.

Parathyroid carcinoma is an exceedingly rare clinical entity<sup>(1)</sup>. The etiology of parathyroid carcinoma is unknown. It is associated with germline and a somatic mutation in the putative tumor suppressor gene *HRPT2*, which encodes for nuclear parafibromin protein<sup>(1,9)</sup>. Other previous reports have suggested that a history of neck irradiation<sup>(10)</sup>, long standing secondary hyperparathyroidism and end stage renal disease<sup>(11)</sup> increased the risk of parathyroid carcinoma. In addition, mutation of cyclin D1 (CCND1)<sup>(12)</sup> and *HRPT2* (*CDC73*) genes<sup>(13)</sup> also increased the risk of parathyroid carcinoma.

The diagnosis of parathyroid carcinoma can only be confirmed by histopathology, which cannot be replaced by any other diagnostic tools<sup>(14)</sup>. In 1973, Schantz and Castleman<sup>(15)</sup> established a set of histologic criteria for the pathological diagnosis of parathyroid carcinoma. These diagnostic features included uniform sheets of cells arrange in a lobular pattern separated by dense fibrous trabeculae, a thick capsule, atypia of the nucleus and high mitotic rates. However, none of these criteria clearly lead to definite diagnosis. The most definitive diagnostic criteria for parathyroid carcinoma are vascular or capsular invasion, adjacent tissues or regional lymph nodes invasion and distant metastases<sup>(15)</sup>. Moreover, higher expression of Ki-67, lower expression of p27kip1, and cyclin D1 over expression have been demonstrated in carcinoma at a higher extent than that those in adenoma/hyperplasia<sup>(16)</sup>. This type of cancer has a poor prognosis. Specific factors that are independently associate with increase mortality include advanced age, male sex and the presence of distant metastases<sup>(17)</sup>. Neither tumor size nor lymph node status is significant prognostic factor<sup>(18)</sup>.

To date, surgery is the only definitive and curative management of parathyroid carcinoma. Localizing the tumor prior to surgery is obligatory in primary hyperparathyroidism patients who are suspected of having parathyroid carcinoma. Traditional localization techniques with ultrasonography, computerized tomography or MRI scans can be used but none could lead to a definite diagnosis of parathyroid carcinoma. With these imaging options, signs of local infiltration, distant metastasis or lymph node spread may demonstrate and would enhance the suspicion of parathyroid carcinoma<sup>(19,20)</sup>. Sestamibi scintigraphy can demonstrate a wide field of view to assess the ectopic parathyroid gland or any distant metastases(21) but provides less information in term of local extension. Because surgery is the only curative treatment, the cornerstone of treatment is to remove all the tumor for the prevention of local recurrence



Fig. 4 Algorithm of diagnosis and treatment of this reported case.

and to lower the risk of distant metastases from the persistent disease<sup>(1)</sup>. The surgical approach can be categorized into local excision and en bloc resection of the tumor with ipsilateral hemithyroidectomy and centrocervical lymphadenectomy. The en bloc resection should be performed as the minimum surgical approach in all patients suspected of having parathyroid carcinoma. Therefore, the specific clinical parameters to determine the risk of cancer should be assessed prior to surgery because the surgical approach is irreversible and the morbidity is increased after the second operation<sup>(5)</sup>.

The hypercoagulable state is frequently found in paraneoplastic syndrome, which usually presents with deep vein thrombosis and pulmonary embolism. Malignant diseases increase the risk of thrombosis 4.1 folds<sup>(7)</sup>. From a cohort study, approximately 10% of patients presenting with idiopathic thromboembolism are subsequently diagnosed with cancer over the next 5 to 10 years<sup>(22)</sup>. The clinical presentation of pulmonary embolism ranges from sustained hypotension to subtle clinical findings or patients are completely asymptomatic. Patients with deep vein thrombosis have a high incidence of asymptomatic pulmonary embolism. Due to the high incidence of asymptomatic pulmonary embolism in deep vein thrombosis, pulmonary embolism may commonly occur but infrequently leads to death<sup>(23)</sup>. Nevertheless, pulmonary embolism is the leading cause of unsuspected death in hospitalized patients<sup>(24)</sup>. The incidentally found asymptomatic subclavian vein thrombosis and pulmonary embolism in the patient in the present study led to a strongly suspected diagnosis of parathyroid carcinoma. The subclavian vein thrombosis found in this patient occurred on the contralateral side to the parathyroid tumor. Hence, it is less possible that the subclavian vein thrombosis arose as a result of the local effect of the tumor. The pathological fracture found in the right proximal humerus of this patient may lead to local vascular thrombosis. Sawyer et al<sup>(25)</sup> showed that the humeral fracture per se can induce brachial vein thrombosis due to immobilization and local trauma from the fracture bone adjacent to the vessel wall<sup>(25)</sup>. To date, subclavian thrombosis due to a humeral fracture has never been reported. Therefore, anatomically, the occurrence of the subclavian vein thrombosis was unlikely to result from the humeral fracture. In addition to supporting the clinical diagnosis of parathyroid carcinoma, this venous thromboembolism in this patient broadened the spectrum of systemic manifestation of this carcinoma.

According to published literature available on MEDLINE, there was only one case report illustrating venous thromboembolism in cases of parathyroid carcinoma. Marrahi et al<sup>(8)</sup> described a case of parathyroid carcinoma with pulmonary thromboembolism. The symptoms in the patient in their report firstly manifested themselves as associated to pulmonary embolism, including dyspnea and pleuritic chest pain, suggesting a hypercoagulable state. In addition, following further exploration, a palpable neck mass with primary hyperparathyroidism was shown. This palpable neck mass was illustrated as a 2.6x2.7 cm, malignant suspicious mass seen using cervical ultrasonography, as well as a functioning mass in the 99mTc MIBI scintigraphy, suggesting parathyroid neoplasm. The first presentation of venous thromboembolism in their patient triggered the diagnosis of malignant disease with paraneoplastic syndrome, and then led to the further exploration to identify the primary cancer. The combination of primary hyperparathyrodism with a palpable neck mass and radioimaging findings raised a suspicion of parathyroid carcinoma as a primary cancer. On the contrary, our report showed a patient who condition firstly manifested itself with overt hyperparathyroid bone disease. Further exploration gave information including palpable neck mass, nephrocalcinosis with renal impairment, as well as extremely high calcium and parathyroid levels, raising the clinical suspicion of parathyroid carcinoma as the cause of hyperparathyroidism. However, without the pathological specimen, the definite diagnosis of parathyroid carcinoma could not be established. The incidentally found subclavian vein thrombosis and pulmonary embolism indicated a paraneoplastic syndrome of hypercoagulability in the present patient, which, in turn, strikingly increased the likelihood of diagnosis of parathyroid carcinoma. Indeed, venous thromboembolism in either previous case report or in our patient was an essential clue to establishing the clinical diagnosis of parathyroid carcinoma. Venous thromboembolism may be asymptomatic but it can help in diagnosis of parathyroid carcinoma. A CT scan including the neck and chest may be an appropriate imaging option for establishing the diagnosis of parathyroid carcinoma, especially in doubtful situations. The preoperative diagnosis of parathyroid carcinoma would lead to a better chance of a cure because the only curative treatment available is en bloc surgery, which is not usually carried out in cases of parathyroid adenoma

The mechanism of hypercoagulability in primary hyperparathyroidism has not been well understood. Hypercalcemia per se can induce a hypercoagulable state according to studies in animal models<sup>(26,27)</sup>. In addition, dehydration and hemoconcentration associated with hypercalcemia have been proposed as potentiate factors for the development of thromboembolism<sup>(28)</sup>. Chappel and Farrington<sup>(29)</sup> reported arterial ischemic optic neuropathy in a parathyroid adenoma patient who had severe hypercalcemia (serum calcium levels of 14.7 mg/dL) and extremely high parathyroid

hormone levels (PTH of 820 pg/ml). Walker et al<sup>(30)</sup> demonstrated cerebral infarction secondary to internal carotid artery spasm in iatrogenic hypercalcemia (serum calcium of Ca 14.4 mg/dL). Multiple mechanisms have been proposed for hypercalcemiainduced arterial insufficiency, including vascular calcification, and vasospasm due to increase in intracellular free calcium levels on the actin-myosin coupling in smooth muscle cell contraction<sup>(29)</sup>. Nevertheless, this proposed mechanism of arterial thrombosis may not be applied for the pathogenesis of venous thromboembolism. In addition to hypercalcaemia, the nature of the carcinoma also has a strong correlation with hypercoagulability. The expressed tissue factors by the tumor cells play a prominent role in inducing the hypercoagulation state. These tissue factors can up-regulate vascular endothelial growth factor (VEGF) and activate protease activated receptor 2 (PAR-2), which are activators of the coagulation system<sup>(31)</sup>. Parathyroid carcinoma cells themselves may express factors that can activate the coagulation cascades; however, information in this particular issue is still lacking. Although the mechanism of hypercoagulability in parathyroid carcinoma remains to be elucidated, the authors' report, in combination with the previous report, demonstrated that hypercoagulability was one of the systemic manifestations of parathyroid carcinoma and a helpful clue in establishing the diagnosis of this carcinoma.

#### Conclusion

The authors presented the case with the overt clinical symptoms of hyperparathyroidism and a palpable neck mass, indicating a preferred diagnosis of parathyroid carcinoma to adenoma. Subsequently an asymptomatic venous thromboembolism was found in the computerized tomography providing an important clue for establishing the diagnosis of parathyroid carcinoma preoperatively. The preoperative clinical diagnosis of carcinoma led to a curative surgical plan by parathyroidectomy, hemithyroidectomy and central lymphadenectomy. This surgical approach was essential for the curative outcome as indicated during the follow-up period. Venous thromboembolism can be symptomatic and may have a higher prevalence than that expected by the authors, and the exploration of this phenomenon may help the preoperative diagnosis which then would lead a more radical surgery than that in parathyroid adenoma. Therefore, in equivocal cases, computerized tomography of the neck and chest may be an appropriate choice of imaging for establishing a clinical diagnosis of parathyroid carcinoma. The computerized tomography of the neck including the chest has an advantage over the ultrasonography or scintigraphy, because it can demonstrate not only the local invasion of the tumor but also other systemic manifestations of the tumor.

#### What is already known on this topic?

Paraneoplastic syndrome is a rare manifestation of parathyroid carcinoma. Parathyroid carcinoma usually presents with the clinical symptoms related to severe hypercalcemia, overt bone disease and renal stone disease, in combination with palpable neck mass and symptoms related to local mass effects, such as recurrent laryngeal nerve palsy or local neck pain. Either ultrasonography or scintigraphy is mandatory diagnostic imaging technique to localize the neoplasm.

#### What this study adds?

Venous thromboembolism is one of the clinical manifestations of paraneoplastic syndrome in parathyroid carcinoma, and may occur without symptoms. The venous thromboembolism provides an important clue for establishing the diagnosis of parathyroid carcinoma. Because this event can be asymptomatic but essential to establishing the diagnosis of carcinoma, the computerized tomography of the neck including the chest would be considered as a helpful tool to establish the diagnosis of parathyroid carcinoma especially in a doubtful situation.

#### Potential conflicts of interest

None.

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## ภาวะลิ่มเลือดอุดตันที่ปอดและหลอดเลือดดำ subclavian ในผู้ป่วยมะเร็งของต่อมพาราไทรอยด์: รายงานผู้ป่วย 1 ราย และทบทวนวรรณกรรม

### วรผกา มโนสร้อย, คมสันต์ วรรณไสย, เมตตาภรณ์ พิมพ์พิไล

มะเร็งของต่อมพาราไทรอยด์เป็นสาเหตุที่พบได้ไม่บ่อยของภาวะฮอร์โมนพาราไทรอยด์สูง โดยพบว่าเป็นสาเหตุของการ มีภาวะฮอร์โมนพาราไทรอยด์สูงเกินแบบปฐมภูมิเพียงร้อยละ 0.4-5.2 อาการสำคัญที่ทำให้น่าสงสัยถึงมะเร็งชนิดดังกล่าว ได้แก่ การพบก้อนที่คลำได้ที่บริเวณลำคอร่วมกับการพบลักษณะการเปลี่ยนแปลงของกระดูกอย่างรุนแรง หรือ การมีโรคทางไตที่เกิดจาก การมีฮอร์โมนพาราไทรอยด์สูง หรือ การมีระคับแคลเซียมในเลือดที่สูงอย่างรุนแรงร่วมกับการมีระดับฮอร์โมนพาราไทรอยด์ที่สูงมาก แต่อย่างไรก็ตามการตรวจชิ้นเนื้อทางพยาธิวิทยาก็เป็นเพียงวิธีการเดียวที่จะยืนยันการวินิจฉัยมะเร็งของต่อมพาราไทรอยด์ได้ ในปัจจุบันการผ่าตัดเพื่อนำมะเร็งออกทั้งหมดเป็นการรักษาเพียงชนิดเดียวที่จะยืนยันการวินิจฉัยมะเร็งของต่อมพาราไทรอยด์ได้ ในปัจจุบันการผ่าตัดเพื่อนำมะเร็งออกทั้งหมดเป็นการรักษาเพียงชนิดเดียวที่จะทำให้หายขาดจากโรคได้ ดังนั้นการตรวจวินิจฉัยว่า เป็นมะเร็งก่อนการผ่าตัดจึงเป็นสิ่งที่สำคัญที่นำไปสู่การวางแผนการรักษาที่เหมาะสม รายงานผู้ป่วยนี้ได้รายงานผู้ป่วยมะเร็งของ ต่อมพาราไทรอยด์ที่มีกาวะลิ่มเลือดอุดตันที่ปอดและหลอดเลือดดำ subclavian โดยที่ไม่ปรากฏอาการซึ่งแสดงถึงภาวะเลือด แข็งตัวมากผิดปกติซึ่งพบได้ในกลุ่มโรคมะเร็ง โดยการพบภาวะเลือดแข็งตัวมากผิดปกติในผู้ป่วยรายนี้ซึ่งเป็นผู้ป่วยที่มีอาการแสดง ที่รุนแรงของการมีฮอร์โมนพาราไทรอยด์สูงเกินร่วมกับก้อนบริเวณลำคอ เป็นการบ่งชี้ถึงการวินิจฉัยว่าสาเหตุของภาวะฮอร์โมน พาราไทรอยด์สูงเกินเกิดจากมะเร็งของต่อมพาราไทรอยด์ การวินิจฉัยมะเร็งของต่อมพาราไทรอยด์ตั้งแต่ก่อนผ่าตัดนี้สามารถ นำไปสู่การผ่าตัดที่เหมาะสมเพื่อนำมะเร็งออกทั้งหมดเนื่องจากภาวะลิ่มเลือดอุตดันที่ปอดและที่หลอดเลือดดำอาจไม่ปรากฏ อาการแสดงที่ชัดเจน ดังนั้นการถวินิจฉัยมะเร็งพวิดจิตจากภาวะลิ่มเลือนจากรล่งอย่งข้อเร่ารวินิจฉัยของมะเร็งก่อนกัรกอ โดยเลพาะอย่งยิ่งในกรณีที่ไม่สามารถวินิจฉัยมะเร็งพิจดจากภาวะลิ่มเลือดจุนจากหลักฐานอง่งยั่งผู้กลารวินิจฉัยมะเร็งกัดได้ โดยเฉพาะอย่งยิ่งในกรณีที่ไม่สามารถวินิจฉัยมะเร็งพิจดจากวได้อย่างชัดเจนจากหลักฐานองกัลอีนๆ ๆ