Case Report

Primary Hyperparathyroidism Due to Cystic Parathyroid Adenoma: A Case Report

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Raw Cystic parathyroid adenoma is a rare cause of primary hyperparathyroidism. The authors report one case of cystic parathyroid adenoma, who presented with progressive right hip pain for one year. The patient had severe hypercalcemia at the first presentation and was misdiagnosed as having metastatic cancer at first. An iliac bone biopsy was performed and showed a giant cell tumor. Parathyroid hormone level was evaluated later and was found to be high, 1,555 pg/ml (15-65 pg/ml). An MRI study of the neck was done and revealed a cystic mass 38x36x40 mm in diameter just below the left lower pole of the thyroid gland. Tc-99m MIBI scan demonstrated increase and retention of radioactivity uptake at the same area. Hyperfunctioning parathyroid gland was considered. Parathyroidectomy was done and histopathology revealed cystic parathyroid adenoma. Serum calcium was normal and hip pain was markedly improved after the surgery.

Keywords: *Cystic parathyroid adenoma, Primary hyperparathyroidism*

J Med Assoc Thai 2007; 90 (Suppl 2): 79-84
Full text. e-Journal: *http://www.medassocthai.org/journal*

Primary hyperparathyroidism is usually caused by a parathyroid adenoma, occasionally by parathyroid hyperplasia, and rarely by a parathyroid cyst or parathyroid carcinoma. Parathyroid cysts are a rare cause of the neck mass and were first described by Sanstrom in 1880. The majority of these cysts are nonfunctioning; however, 10-17% may function. The authors report a case of cystic parathyroid adenoma caused primary hyperparathyroidism and review of the relevant literature.

Case Report

A forty- five year old woman presented with progressive right hip pain for one year. She had had a history of benign tumor and had undergone hysterectomy and bilateral oophorectomy 20 years and 15 years ago, respectively. Hormonal replacement therapy with conjugated equine estrogen 0.625 mg daily had been prescribed and stopped two years before this presentation. On examination, she was alert. No lymphadenopathy or bony tenderness. The breasts had no mass and neurological examination was normal. Film of the pelvis showed multiple areas of osteolytic lesion. At the presentation, her calcium level was 14.9 mg/dl, phosphorus 3.1 mg/dl, albumin 4.3 g/dl. Her renal function was mildly impaired; creatinine level was 1.9 mg/dl, due to prerenal azotemia. She was at first misdiagnosed as having metastatic cancer. The primary site of cancer was sought without success. Right iliac bone biopsy revealed a giant cell tumor grade I-II with secondary aneurysmal bone cyst change. The parathyroid hormone level was 1,555 pg/ml (15-65 pg/ml). The patient was diagnosed as having primary hyperparathyroidism and an endocrinologist consultation was made. Bone survey was performed. Skull x-ray showed salt and pepper appearance. Resorption at the radial side of second to fifth distal phalanges of both hands was demonstrated on hands x-ray. Bone mineral density showed osteoporosis predominated at cortical bone. T-score was -4.1 at femur, -4.1 at radius and -2.7 at lumbar region respectively. Tc-99m MIBI scan demonstrated increased radioactivity uptake at lower pole of left lobe of thyroid gland. The delayed MIBI imaged

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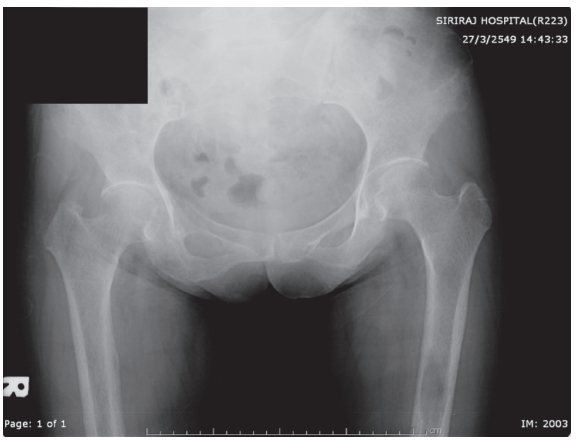

Fig. 1 Film pelvis showed multiple areas of osteolytic lesion

showed retention of radioactivity at the same area in which the hyperfunctioning parathyroid gland was considered. The MRI study of the neck revealed a soft tissue mass situated just below the thyroid gland, 38x36x40 mm. in size, with heterogeneous low signal intensity on T1WI and increase signal intensity on T2WI. Rim enhancement was seen after gadolinium injection. The hypointense part of T2WI probably represented the cystic portion, the mass was well-defined and had a smooth border without invasion to the adjacent structure. There was no lymphadenopathy or vascular invasion. Cystic parathyroid adenoma was considered and an operation was performed after correction of hypercalcemia and other metabolic abnormalities. During the operation, a 3 cm-mass with cystic component and yellowish content was found. There was no lymphadenopathy. The rest of the parathyroid glands and the thyroid gland were normal. The mass was surgically removed and tissues were sent for pathological examination. Sections revealed a parathyroid neoplasm, 4.5x3.3x2 cm in size, composed of chief cells proliferation with focal atypical nuclei. No capsular or surrounding tissue invasion could be identified. Broad fibrous bands were focally seen. Mitotic figures, tumor necrosis, or macronuclei were not present. MIB-1 averages 1-2%. Sixteen hours after the operation, the PTH level declined to 70.89 pg/ml. Calcium level was measured every 6 hours as hungry bone syndrome was expected. The patient developed tetany approximately 24 hours after the operation. The serum calcium and phophorus were 7.8 and 2 mg/dl respectively. Calcium carbonate and 1,25 dihydroxy vitamin D were given. The dose was titrated up to eradicate the tetany symptoms and she was discharged 10 days after the operation with calcium carbonate 8 gm/day and 1,25 dihydroxy vitamin D 0.5 μg/day. Her calcium level was 7.9 mg/dl on the discharged date. After 4 months of the follow-up, the patients remain normocalcemia, hip pain was markedly improved but PTH level had risen to 240 pg/ml.

Discussion

Macroscopic parathyroid cyst is a rare clinical entity and less than 300 cases have been reported. Ippontito et al reported 38 non-functional parathyroid cysts in 2,505 parathyroidectomies performed in 25 years[1]. It represented 1% of all cystic lesions of the neck[2]. Mediastinal localization has been reported in up to 30% of the cases[3].

The pathogenesis of parathyroid cysts remains unclear. Four hypotheses have been postulated.

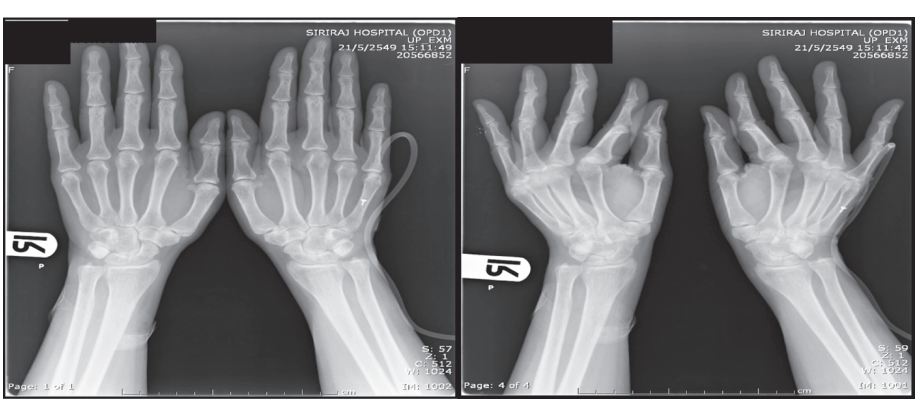

Fig. 2 Hand x-ray demonstrated resorption at the radial side of second to fifth distal phalanges of both hands

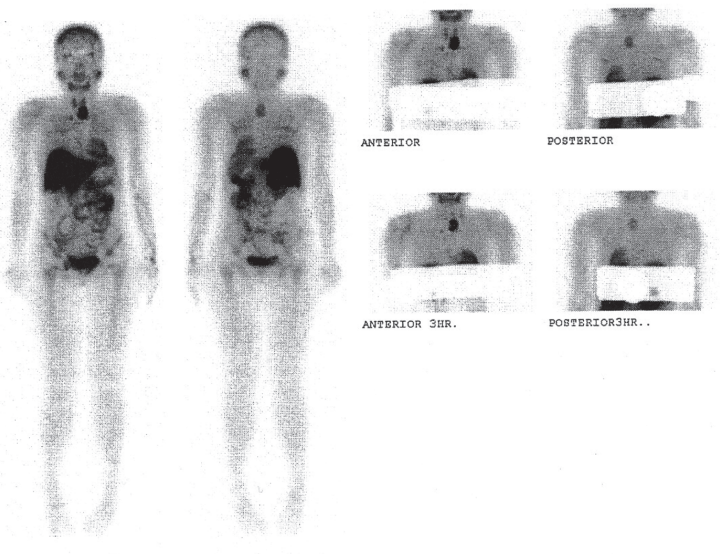

Fig. 3 Tc-99m MIBI scan showed increased radioactivity uptake at lower pole of left lobe of thyroid gland. The delayed MIBI imaged showed retention of radioactivity at the same area

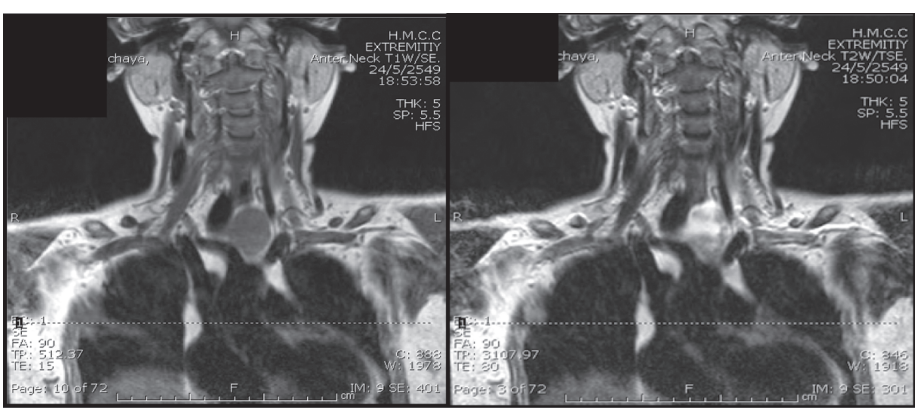

Fig. 4 MRI study of the neck revealed cystic soft tissue mass situated just below the thyroid gland, 38x36x40 mm in size Heterogeneous low signal intensity on T1WI and increase signal intensity on T2WI

1. Parathyroid cyst may develop from persistent embryonic remnants. The superior glands developed from the fourth branchial clefts, whereas the inferior glands originated from the third branchial pouches. In 1939, Gilmour documented that the developing parathyroid has cystic components that may persist in many adults[4]. Therefore, cystic parathyroid masses could be an enlargement of the existing glands.

2. The coalescence of multiple parathyroid microcysts. One autopsy series reported by Black and Watts showed that 44% (42 of 96 cadavers) had microcysts less than 1 mm. in diameter, and 6% (6 cadavers) have microcysts of 1 mm. or more[5]. This study, in agreement with other studies, shows that the estimated prevalence of microcysts is 5-50% of normal parathyroid glands.

3. An enlargement of one large microcyst has also been postulated to cause parathyroid cysts[5].

4. The cystic degeneration of the parathyroid glands which is common in parathyroid adenomas or hyperplastic glands[6-8].

Whether there is a genetic predisposition to cystic parathyroid disease is uncertain. The evidence

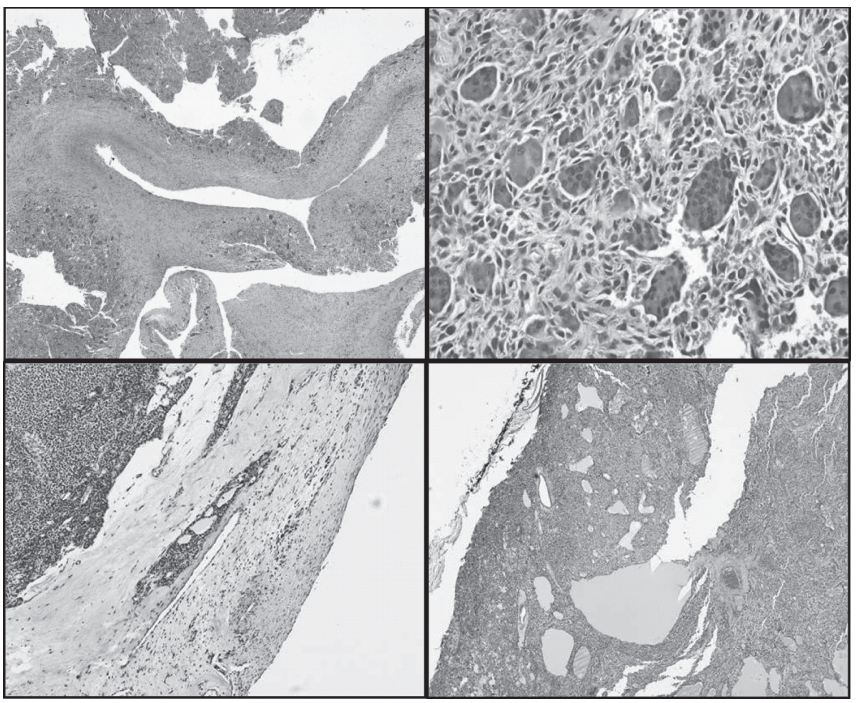

Fig. 5 Right iliac bone biopsy showed giant cell tumor grade I-II with secondary aneurysmal bone cyst change

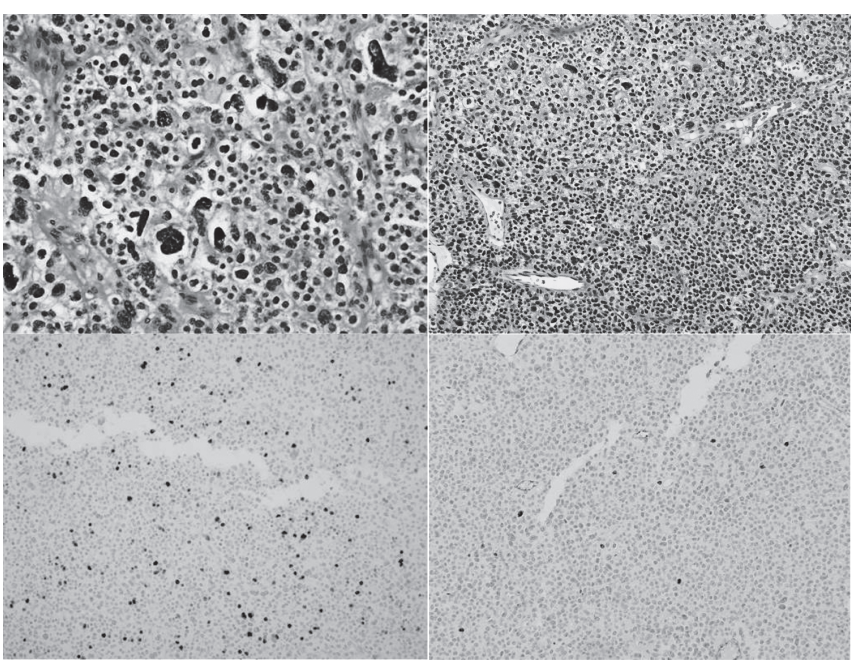

Fig. 6 Sections showed parathyroid neoplasm, 4.5x3.3x2 cm in size, composed of chief cell proliferation with focal atypical nuclei. No capsular or surrounding tissues invasion could be identified. Broad fibrous bands were focally seen. Mitotic figures, tumor necrosis, macronuclei were not present. MIB-1 averages 1-2%

to support a genetic role has been provided by Mallette et al who reported a family of four patients with cystic hyperparathyroidism[9].

Parathyroid cysts have been divided into functional cysts and non-functional cysts depending on their association with hypercalcemia. Ten to seventeen percent of the parathyroid cysts have been reported to be functional.

Non-functional parathyroid cysts mostly presented in middle aged women. The female to male ratio is 2.5:1. They are usually asymptomatic and may be discovered incidentally on a routine clinical examination or chest X-ray[1]. The inferior parthyroid glands are the most common sites[10]. The cysts occasionally cause compressive symptoms, such as dysphagia, dyspnea, hoarseness and pain, especially when located in the mediastinum. On examination, parathyroid cysts tend to be soft, mobile and not tender, located in the lower part of the neck but can also occur at any site between the jaw and the mediastinum[11,12]. If a thyroid scan was performed, it would show an area of absence uptake. Tl^{201}-Tc-^{99m} pertechnetate subtraction or sestamibi scintigraphy rarely yields positive results. Imaging studies such as ultrasonography, CT and MRI may demonstrate the cystic nature of these lesions but are usually unable to determine the exact pathology[13]. Fine needle aspiration is the main diagnostic tool. The characteristic of the aspiration fluid is clear and colourless with high intact PTH and c-terminal PTH level which is many times above serum PTH level. Thyroglobulin and calcitonin level should be immeasurable, in contrast to thyroid cysts which have high thyroglobulin concentration and low or undetectable PTH level[14].

Functioning parathyroid cysts are parathyroid cysts which caused primary hyperparathyroidism. A series of 813 parathyroidectomies for primary hyperparathyroidism at the Mayo clinic showed that 3% (21) of the cases were cystic in nature. Two separate studies[8,15] also reported a 3-4% rate of parathyroid cysts in their parathyroidectomies for primary hyperparathyroidism. Chigot et al showed an increased incidence of cystic primary hyperparathyroidism in the elderly[16]. The functional cysts are more common in males and occur less frequently than non-functional cysts. De Ridder et al[17] reported that only 17% (27/157) of the cysts removed were functional and that the most common cause was cystic degeneration of the parathyroid adenoma[18]. The patients could be presented as symptomatic hypercalcemia, hypercalcemic crisis, recurrent stone formation, neck mass or bone and joint pain. Parathyroid cancer deriving from functional parathyroid cyst has also been reported[19]. Some authors suggested that functional cysts are a different entity. They classified functional cysts as pseudocysts caused by cystic degeneration of the parathyroid adenoma and non-functional cysts as the true parathyroid cysts[14,20-22].

Treatment of parathyroid cyst includes aspiration, injection of sclerosing agents or surgical excision. Fine needle aspiration may be curative in some of the non-functional cysts but surgery appears to be the treatment of choice for functional parathyroid cysts.

Conclusion

Cystic parathyroid adenoma is rare and is an unusual cause of primary hyperparathyroidism. It occurs more often in men and is more likely to be caused by degenerative changes of a parathyroid tumor. The authors reported a case of cystic parathyroid adenoma with primary hyperparathyroidism in a woman who presented with hip pain, multiple osteolytic lesions and hypercalcemia mimicking metastatic cancer. Serum and cystic fluid examination for PTH level help with the diagnosis. Surgical removal is the treatment of choice.

Acknowledgement

The authors wish to thank Dr. Soranart Muangsomboon, Department of Pathology, Siriraj Hospital, for providing the histologic Fig. 5 and 6.

References

1. Ippolito G, Palazzo FF, Sebag F, Sierra M, De Micco C, Henry JF. A single-institution 25-year review of true parathyroid cysts. Langenbecks Arch Surg 2006; 391: 13-8.
2. Silverman JF, Khazanie PG, Norris HT, Fore WW. Parathyroid hormone (PTH) assay of parathyroid cysts examined by fine-needle aspiration biopsy. Am J Clin Pathol 1986; 86: 776-80.
3. Shields TW, Immerman SC. Mediastinal parathyroid cysts revisited. Ann Thorac Surg 1999; 67: 581-90.
4. Gilmour JR. The normal histology of parathyroid glands. J Pathol Bacteriol 1939; 48: 187-222.
5. Black BM, Watts KF. Cysts of parathyroid origin: report of two cases and study of incidence and pathogenesis of cysts in parathyroid glands. Surgery 1949; 25: 941-9.
6. Crile G Jr, Perryman RG. Parathyroid cysts: report of five cases. Surgery 1953; 34: 151-4.
7. Clark OH. Parathyroid cysts. Am J Surg 1978; 135: 395-402.

8. Calandra DB, Shah KH, Prinz RA, Sullivan H, Hofmann C, Oslapas R, et al. Parathyroid cysts: a report of eleven cases including two associated with hyperparathyroid crisis. Surgery 1983; 94: 887-92.
9. Mallette LE, Malini S, Rappaport MP, Kirkland JL. Familial cystic parathyroid adenomatosis. Ann Intern Med 1987; 107: 54-60.
10. Bondeson AG, Thompson NW. Mediastinal parathyroid adenomas and carcinomas. In: Shields TW, editor. Mediastinal surgery. Philadelphia: Lea & Febiger; 1991: 289-95.
11. Jha BC, Nagarkar NM, Kochhar S, Mohan H, Dass A. Parathyroid cyst: a rare cause of an anterior neck mass. J Laryngol Otol 1999; 113: 73-5.
12. Haid SP, Method HL, Beal JM. Parathyroid cysts. Report of two cases and a review of the literature. Arch Surg 1967; 94: 421-6.
13. Pacini F, Antonelli A, Lari R, Gasperini L, Baschieri L, Pinchera A. Unsuspected parathyroid cysts diagnosed by measurement of thyroglobulin and parathyroid hormone concentrations in fluid aspirates. Ann Intern Med 1985; 102: 793-4.
14. Hoehn JG, Beahrs OH, Woolner LB. Unusual surgical lesions of the parathyroid gland. Am J Surg 1969; 118: 770-8.
15. Rosenberg J, Orlando R 3rd, Ludwig M, Pyrtek LJ. Parathyroid cysts. Am J Surg 1982; 143: 473-80.
16. Chigot JP, Menegaux F, Achrafi H. Should primary hyperparathyroidism be treated surgically in elderly patients older than 75 years? Surgery 1995; 117: 397-401.
17. de Ridder VA, Brom HL, Blok P. Hyperparathyroidism due to primary cystic parathyroid adenoma. Neth J Surg 1986; 38: 134-7.
18. Inoue H, Wakabayashi Y, Konishi T, Okada Y, Takeuchi H, Tomoyoshi T. A parathyroid cyst and an adenoma associated with primary hyperparathyroidism: report of a case. Hinyokika Kiyo 1990; 36: 1197-202.
19. Pirundini P, Zarif A, Wihbey JG. A rare manifestation of parathyroid carcinoma presenting as a cystic neck mass. Conn Med 1998; 62: 195-7.
20. Troster M, chiu HF, McLarty TD. Parathyroid cysts: report of a case with ultrastructural observations. Surgery 1978; 83: 238-42.
21. Armstrong J, Leteurtre E, Proye C. Intraparathyroid cyst: a tumour of branchial origin and a possible pitfall for targeted parathyroid surgery. ANZ J Surg 2003; 73: 1048-51.
22. Haugen OA. Parathyroid cysts. Acta Chir Scand 1970; 136: 247-9.

Primary hyperparathyroidism จาก cystic parathyroid adenoma: รายงานผู้ป่วยหนึ่งราย

นันทกร ทองแตง, ณัฐเชษฐ์ เปล่งวิทยา, ระวีวรรณ เสิศวัฒนารักษ์, ธวัชชัย พีรพัฒน์ดิษฐ์

Cystic parathyroid adenoma เป็นสาเหตุของภาวะ primary hyperparathyroidism ที่พบได้น้อยมาก ผู้ศึกษาได้รายงานผู้ป่วยหนึ่งรายที่มีอาการปวดสะโพกขวามาเป็นเวลาหนึ่งปี ขณะมาพบแพทย์ผู้ป่วยมีระดับแคลเซียมในเลือดสูงมากและถูกวินิจฉัยในตอนแรกว่าเป็นมะเร็งกระจายมาที่กระดูก ภายหลังการตรวจชิ้นเนื้อที่กระดูกเชิงกรานและตรวจระดับฮอร์โมนพาราไทรอยด์ (parathyroid hormone) ในเลือด จึงวินิจฉัยว่าผู้ป่วยมีแคลเซียมในเลือดสูงจากภาวะ primary hyperparathyroidism ผลการตรวจ MRI ที่คอพบถุงน้ำ (cyst) ที่ตำแหน่งต่อมพาราไทรอยด์ด้านซ้ายล่างผล Tc-99m MIBI scan ยืนยันการวินิจฉัยดังกล่าว ผู้ป่วยได้รับการรักษาโดยการผ่าตัด ผลการตรวจทางพยาธิวิทยาเข้าได้ กับภาวะ cystic parathyroid adenoma ภายหลังการผ่าตัดอาการปวดสะโพกขวาของผู้ป่วยดีขึ้นมากจนกลับมาเดินได้ และระดับแคลเซียมในเลือดกลับมาสู่ปกติ