A Case of Secondary Erythermalgia Associated with Hypertension

Jin Young Park, M.D., Tae Yoon Kim, M.D., Hyun Jeong Lee, M.D., Sang Chin Lee, M.D., Si-Yong Kim, M.D.

Department of Dermatology, College of Medicine, The Catholic University of Korea, Seoul, Korea

Erythermalgia(Erythermalgia) is a syndrome of red, warm, congested, and burning painful extremities. Presently, there are three distinct clinicopathological entities: erythermalgia, primary erythermalgia, and secondary erythermalgia. Secondary erythermalgia usually arises at an adult age either in association with a detectable underlying disorder or with the use of vasoactive drugs. Typically, it responds to proper treatment of the underlying disorder or discontinuation of the causative drugs.

A seven-year-old boy presented with persisting burning pain, erythema, and warmth on both of his feet and lower legs, along with hypertension. He had had this condition for 20 months. Laboratory studies of the patient revealed increased urinary catecholamines and plasma renin activity. Various treatment modalities including aspirin, captopril, sodium nitroprusside, labetalol, epidural block, and stellate ganglion block yielded unfavorable results.


Key Words: Secondary erythermalgia, Hypertension

Secondary erythermalgia may occur in association with a detectable underlying disorder or with the use of vasoactive drugs. Typically, the syndrome occurs in adults and responds to proper treatment of the underlying disorder or discontinuation of the incriminating drugs. Since 1979, seven cases of acute secondary erythermalgia associated with hypertension have been reported in children. They were transient with no relapse. In Korea, four cases of erythermalgia have been reported: three were primary erythermalgia and one was secondary erythermalgia associated with bronchial asthma.

We report a rare intractable case of secondary erythermalgia in a child associated with hypertension.

CASE REPORT

A seven-year-old Korean boy had suffered from burning pain on both feet, progressively spreading to the ankles and lower legs since the age of five. The pain occurred in association with redness, warmth, and swelling of the feet. Exercise and exposure to heat intensified the symptoms while immersing the feet in ice-cold water offered temporary and slight relief. Recently, the patient's symptoms had been so aggravated that he had to immerse his feet in cold water all day long. There was nothing significant in his past medical and family history.

A physical examination revealed persistent and symmetric discoloration of dark red to purple on both feet and lower legs as well as a firm pitting edema(Fig.1). The affected extremities were warm. Lichenification and several small ulcers were found on the feet and ankles, and perhaps the latter resulted from attempts to control pain by constantly immersing the feet in cold water. The recurrent secondary infection of the patient's feet may be attributable to the same cause. The

Received November 7, 1997.
Accepted for publication February 12, 1998.
Reprint request to: Jin Young Park, M.D., Department of Dermatology, College of Medicine, The Catholic University of Korea, Seoul, Korea

101
patient showed growth retardation: weight, height, and head circumference were within the 3rd percentile, and chest circumference was within the 25th percentile. Blood pressure was measured at 180-200 mmHg in systole and 100-120 mmHg in diastole.

Laboratory data, including an antinuclear antibody, rheumatoid factor, cold agglutinin, cryoglobulin, C1, C3, urinalysis, electrolyte, liver function test, kidney function test, thyroid function test, chest x-ray, electrocardiography, and echocardiography, were all negative or within normal limits. CBC showed mild leukocytosis (12,000-15,700/mm³) and relative thrombocytosis (356-560 × 10⁹/L). Twenty-four hour urine epinephrine was 45.3μg/24hr (normal: 0.2-10μg/24hr); norepinephrine, 183.4μg/24hr (normal: 8-45μg/24hr); and plasma renin activity, 25.31ng/ml/hr (normal; <4.4ng/ml/hr). However, an abdominal ultrasonogram, renal scan with DTPA, abdominal CT, MIBG scan, and intravenous urogram did not reveal any abnormal findings.

A histopathological examination of a skin biopsy specimen from the right lower leg incuding the ulcer showed necrosis of the epidermis with necrotic debris. Telangiectasia and mild perivascular inflammatory infiltrate of lymphocytes in the upper dermis was also noted (Fig. 2).

The patient was initially treated with aspirin (600mg/day) for eight weeks, but there was no improvement. Subsequently oral captopril (12.5mg/day) was administered for two weeks, intravenous sodium nitroprusside (1-5μg/kg/min) for three weeks, an epidural block (bupivacaine, fen-tanyl, morphine) for 10 days, and stellate ganglion block (lidocaine). He was also treated with intravenous labetalol (1mg/kg/hr) for a week and oral labetalol (200mg/day) for three weeks. When sodium nitroprusside and labetalol were used, there was a temporary drop in blood pressure accompanied by hypothermia (34.35.2°C). However, there was no improvement in the erythemalgalic symptoms. Morphine (10mg/day) was used to control the pain, but no improvement was shown. The patient's symptoms were intractable and gradually grew worse. As a consequence of this disabling illness, he was unable to walk and compelled to a sedentary life.

**DISCUSSION**

In 1878, Mitchell coined the term 'erythromelalgia', based on the term proposed by Smith and Allen 'erythralgia' in 1938. Up to now, several classifications for erythromelalgia(erythermalgia) have been proposed by many, among which Drenth and Michiels' proposal seems to be more reasonable. They divided this syndrome into three entities: erythromelalgia, primary erythermalgia, and secondary erythermalgia.

The curable variant, erythromelalgia, is linked to thrombocytosis associated with chronic myeloproliferative disorders. It occurs in adults and the symptoms are unilaterally or asymmetrically distributed. The incurable variant, primary erythermalgia, spontaneously arises in children or adolescents without associated disorders and re-
A Case of Secondary Erythermalgia Associated with Hypertension

reveals bilateral, symmetrical distribution. Along with the hereditary basis of primary erythermalgia, the early and spontaneous onset in life and the persistence throughout life further support the congenital nature of the disease. Secondary erythermalgia is an acquired and potentially curable disease at an adult age. It may be associated with hypertension, systemic lupus erythematosus, rheumatoid arthritis, diabetic neuropathy, and astrocytoma of the brain. In addition, secondary erythermalgia has been detected in patients using nicardipine, nifedipine, bromocriptine, pergolide, and verapamil. Our case showed typical erythermalgia symptoms and hypertension, which is relevant to secondary erythermalgia.

Platelet mediated arteriolar inflammation and thrombosis is understated as the pathogenesis of erythermalgia. The pathogenesis of primary and secondary erythermalgia remains to be elucidated. Sparse autonomic innervation of the arteries and sweat glands in the skin of affected extremities was noted.

In erythermalgia, acetylsalicylic acid may alleviate all symptoms by irreversible inhibition of platelet cyclooxygenase activity. There is no specific treatment for primary erythermalgia, whose symptoms can be minimized by appropriate environmental control with cooling and avoiding heat-producing situations. In secondary erythermalgia, treatment of the underlying disorder or withdrawal of the causative drugs leads to resolution of the clinical symptoms! However, our patient was somewhat peculiar in that his symptoms were intractable to various treatment modalities including low dosage of aspirin, oral captopril, intravenous sodium nitroprusside and labetalol, epidural block, and stellate ganglion block.

Since 1979, seven cases of acute secondary erythermalgia associated with hypertension occurring in childhood were reported. Among them, in four cases, there was a drop in blood pressure and a decrease of erythermalgia symptoms when sodium nitroprusside (1-5 μg/kg/min) was administered intravenously. In each of the other three cases, labetalol (alpha-beta blocker), pizotifen (antiserotonergic drug), and hypnotherapy were effective, respectively. In contrast to primary erythermalgia, the acute episode of secondary erythermalgia was transient with no relapse. But, our patient's symptoms were intractable to various treatment modalities, and only a temporary decrease in blood pressure was noted when sodium nitroprusside and labetalol were administered.

Interestingly, two out of seven patients had elevated urinary catecholamine excretion. In one case, twenty-four hour urinary hydroxyamphetamine acid rose up to 3.5 times above the normal range. In another case, a large increase in normetanephrine (8 × normal), metanephrine (4.1 × normal) and epinephrine and norepinephrine (6.2 × normal) were found. Although these data seem to fit the description of pheochromocytoma, extensive investigations failed to reveal such a tumor. In our case, increased urinary excretion of epinephrine (4.5 × normal) and norepinephrine (4 × normal) was noted, but extensive radiological studies showed no abnormal findings. Although the data needs more precise interpretation, it may provide a possible clue to the nature of the disease. The meaning of increased plasma renin activity (5.75 × normal) remains to be elucidated, too.

Recently, a rare incurable form of secondary erythermalgia occurring in an adult was reported. However, our case is a rare, persisting and yet intractable secondary erythermalgia associated with hypertension, occurring in a child.

REFERENCES

8. Smith LA, Allen EV: Erythermalgia (erythermalgia) of the extremities: A syndrome characterized
by redness, heat and pain. Am Heart J 16:175-188, 1938. (Cited from ref. No. 1)