TOXIC SHOCK SYNDROME ASSOCIATED WITH PHAGE-GROUP-III *STAPHYLOCOCCUS AUREUS*

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INTRODUCTION

Toxic shock syndrome (TSS) was first introduced by Todd and associates (1978). They described a series of 7 children who presented with a prodrome of myalgia. vomiting and diarrhea, followed by high fever, diffuse, desquamating erythroderma, mucous membrane hyperemia and rapid progression to profound hypotension and multisystem dysfunction. They also suggested the association of this syndrome with *Staphylococcus aureus* group I toxin. A similar syndrome has been described earlier by Stevens (1927). In U.S.A. the syndrome was not publicized until September of 1980 when an epidemic occurred in previously healthy young women who used tampons during menstruation (Davis *et al.*, 1980; Shands *et al.*, 1980). Since then more than 1,400 cases of toxic shock syndrome were reported to the Center for Disease Control, U.S.A. Less than 10% of cases were not associated with menstruation. Of these non-menstrual cases, 30% occurred in male patients (Reingold *et al.*, 1982b). The overwhelming majority of the reported TSS cases (97%) occurred in Whites (Reingold *et al.*, 1982a).

A report of a case of TSS associated with an unusual staphylococcus phage type is presented herein.

Report of a Case

A 21-year-old Thai male was admitted to the Ramathibodi hospital, Bangkok on November 16, 1982, with the complaints of fever and rash for two days.

He was been generally healthy until two weeks prior to admission when he noticed a tender and painful mass under his left axilla. Three days before admission, he developed high fever, generalized myalgia, vomiting and few episodes of watery diarrhea. Fever persisted and generalized rash developed the next day. He was then brought to the hospital when his symptoms did not abate.

The patient had no significant past illness except a few episodes of axillary abscesses a few years ago. No history of diabetes mellitus, cigarette smoking or alcohol consumption was noted. He did not have any drug allergy, and none of his household members complained of fever or rash in recent weeks.

On examination the patient appeared acutely ill with temperature of 39.8°C, pulse rate 120/min, the respiration rate 32/min, and blood pressure 80/40 mmHg. He was mildly icteric and had generalized diffuse macular erythroderma and multiple small superficial pustules. Hyperemia of oropharyngeal mucous membrane with strawberry tongue was noted. A left axillary subcutaneous abscess, size 4 × 6 cm was palpable. Both lungs were clear and the heart was normal. The abdomen showed no tenderness or hepatosplenomegaly. Neurological examination was unremarkable.

Urinalysis showed 2+ protein with 30 WBC/HPF and 15 RBC/HPF. The hematocrit was

42%, the white-cell count 21,000/cmm with 87% neutrophils and 10% band forms, the platelet count 240,000/cmm. The total protein was 4.3 gm/dl (albumin 2.0 gm; globulin 2.3 gm), total bilirubin 3.2 mg/dl (direct bilirubin 1.8 mg and the indirect bilirubin 1.4 mg), SGOT 62 units, SGPT 46 units, alkaline phosphatase 0.9 Sigma units, glucose 130 mg/dl, urea nitrogen 21 mg/dl, serum creatinine 1.8 mg/dl, serum calcium 7.0 mg/dl, and phosphorus 2.0 mg/dl, the chest roentgenogram was normal. Gram stain of the pus draining from the left axillary abscess showed gram positive cocci in cluster. The patient was initially diagnosed as having staphylococcal septicemia with shock. Dicloxacillin, 12 gm/day, and gentamicin, 240 mg/day, were promptly started, in addition to fluid replacement. Dopamine infusion was initially needed to maintain his blood pressure. Within 24 hours, his vital signs were stable and dopamine was withdrawn. Incision and drainage of the left axillary abscess was performed. The pus culture subsequently grew *Staphylococcus aureus*, sensitive to methicillin. Three blood cultures and one urine culture yielded no growth. On the first hospital day, he developed right subconjunctival hemorrhage and continued to have vomiting and watery diarrhoea. Three days after admission, the fever, diarrhoea and rash subsided. Gentamicin was discontinued on this day after the negative blood culture results were available. The diagnosis of Toxic Shock Syndrome was considered. On the sixth hospital day, thick desquamation on his extremities and trunk developed. The intravenous antibiotic was replaced by oral diclocil 2 gm/day. Subsequently, laboratory findings returned to normal within one week of hospitalization. The ASO titer was 120 Todd units, VDRL was non-reactive and leptospira titer was negative. He was discharged after two weeks of hospitalization and showed no signs of recurrence or complications when he was examined again one month after discharge.

Staphylococcus aureus isolated from his axillary abscess was phage typed (kindly performed by George Schmid, M.D. from Center for Disease Control, Atlanta, Georgia, U.S.A.) and identified as phage type 6/42E/47/53/54 (group III). This isolate was also demonstrated to produce enterotoxin F.

DISCUSSION

The diagnosis of toxic shock syndrome is usually based on the typical constellation of clinical and laboratory findings because there is still no diagnostic or confirmatory test or marker at the present time. The case report described here is in accordance with the case definition of TSS revised by Center for Disease Control, U.S.A. (Reingold *et al.*, 1982b). Our patient probably represents the first case of TSS in Thailand. Approximately 90% of TSS reported in the United States and Canada are menstrual TSS which is clinically similar to the nonmenstrual type. Surveillance data in U.S.A. showed significant difference in racial distribution among non-menstrual and menstrual TSS. Of the non-menstrual cases, 13% occurred in non-whites compared with 2% of the menstrual cases. Since the proportion on non-menstrual TSS cases in non-whites is similar to their representation in the population in United States, it was suggested that the paucity of menstrual TSS in non-whites was probably due to menstruation related differences and the evidence that tampons are used by significantly more whites than non-white girls (Reingold *et al.*, 1982b). The similar trend of less tampon use is probably true among Thai girls and girls in other Asian countries and the incidence of menstrual TSS in this part of the world would probably be significantly less than their occidental counterpart. Non-menstrual TSS

on the other hand might be increasingly reported with enhanced awareness because the cases are usually associated with non-surgical cutaneous and subcutaneous lesions such as abscesses, ulcers, cellulitis or burns, surgical wound infection, abortion and post partum infection. Among the site of abscess, the extremities, perianal area and the axillae are the commonest (Reingold *et al.*, 1982a).

The case reported herein is most likely a TSS associated with axillary subcutaneous abscess with *Staphylococcus aureus* isolates phage typed 6/42E/47/53/54 (group III). Studies of phage typing of *Staph. aureus* isolates from TSS cases by CDC tindicated that group I phage type 29 and 52 account for 60% of the instances whereas only 10% are due to other groups (Altemeier *et al.*, 1982). The group III staphylococcal isolates from our patient might reflect the difference of predominating phage type *Staphylococcus* in a different geographic area. Further data will be required to appraise this assumption. The finding of enterotoxin F from our staphylococcal isolate is an additional evidence supporting the diagnosis of TSS in our patient because current evidence suggested that pyrogenic exotoxin C or entertoxin F or both may play a vital role in TSS pathogenesis (Altemeier *et al.*, 1982).

In treatment of the TSS cases, it is generally accepted that aggressive measures for treating shock is most important (Chesney *et al.*, 1982). These include intravenous fluid replacement in all patients and use of vasopressor agents in some patients. Antistaphylococcal antibiotics may not affect the outcome of TSS but is still needed to eradicate the primary focus of toxin-producing staphylococci significantly reduce the recurrence rate of TSS. Other potential treatment is the use of intravenous gammaglobulin as a source of antistaphylococcal toxin (Chesney *et al.*, 1982) This approach remains to be further evaluated.

SUMMARY

A case of toxic shock syndrome in a previously-healthy man was reported. The clinical features are in accordance with the criteria of diagnosis defined by the Center for Disease Control (CDC) of USA. Phage-group-III *Staphylococcus aureus*, demonstrated to produce enterotoxin F, was isolated from an axillary abscess.

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REFERENCES

ALTEMEIER, W.A., LEWIS, S.A., SCHLIEVERT, P.M., *et al.*, (1982). *Staphylococcus aureus* associated with Toxic Shock Syndrome. *Ann. Int. Med.*, *96* : 978.

CHESNEY, P.J., CRASS, B.A., POLYAK, M.B., *et al.*, (1982). Toxic Shock Syndrome: Management and long-term sequelae. *Ann. Int. Med.*, *96* : 847.

DAVIS, J.P., CHESNEY, P.J., WAND, P.J., and LAVENTURE, M., (1980). Toxic-Shock Syndrome; Epidemiologic features, recurrence, risk factors, and prevention. *New, Engl. J. Med.*, *303* : 1429.

REINGOLD, A.L., HARGRETT, N.T., DAN, B.N., SHANDS, K.N., STRICKLAND, B.Y. and BROOME, C.V., (1982a). Nonmenstrual Toxic Shock Syndrome: A review of 130 cases. *Ann. Int. Med.*, *96* : 871.

REINGOLD, A.L., HARGRETT, N.T., SHANDS, K.N. *et al.*, (1982b). Toxic Shock Syndrome surveillance in the United States, 1980 to 1981. *Ann. Int. Med.*, *96* : 875.

SHANDS, K.N., SCHMID, G.P., DAN, B.B., *et al.*, (1980). Toxic-Shock Syndrome in menstruating women: association with tampon use and *Staphylococcus aureus* and clinical features in 52 cases. *New Engl. J. Med., 303* : 1436.

STEVENS, F.A., (1927). The occurrence of *Staphylococcus aureus* infection with a scarlatiniform rash. *J.A.M.A., 88*:1957.

TODD, J., FISHAUT , M., KAPRAL, F., WELCH,T.,(1978). Toxic-Shock Syndrome associated with phage-group-I staphylococci. *Lancet, 2* : 1116.