10

Helminth

Strongyloides stercoralis, an intestinal nematode commonly known as the human threadworm, affects millions of people worldwide.[1] It is endemic in Southeast Asia, Latin America, sub-Saharan Africa, and parts of the southeastern USA.[2] In the USA, the highest prevalence rates are found in eastern Kentucky and rural Tennessee. A unique feature of *Strongyloides stercoralis* infection is the occurrence of an autoinfection cycle which permits persistence of the parasite years after the normal host has left an endemic area. In this cycle, the rhabditiform larvae in the duodenojujenal portion of the small intestine transform directly into filariform (infective) larvae. The filariform larvae without leaving the body can reinfect the patient by penetrating the intestinal mucosa. This distinctive characteristic of *Strongyloides*, to persist and replicate within the host for decades, produces minimal or no symptoms. Immunocompromised patients may develop a fulminant illness due to a unique process in the life cycle of *Strongyloides* in which there are dramatic increases in the number of filariform larvae. In the hyperinfection syndrome, massive numbers of larvae migrate through the intestinal mucosa and into the lungs (the usual migration pattern) and disseminate to involve other organ systems not ordinarily a part of the life cycle of the parasite. Larvae may be found in the central nervous system, kidneys, liver, and almost any other organ.

Strongyloides stercoralis hyperinfection syndrome usually develops in the setting of compromised cell-mediated immunity such as severe malnutrition, chronic infection (lepromatous leprosy, human immunodeficiency virus [HIV], tuberculosis, or human T-cell lymphotropic virus type 1 [HTLV]), leukemia, lymphoma, malignancy, or organ transplantation associated with the administration of systemic steroids or other immunosuppressive drugs.[3,4] Hyperinfection syndrome can occur after augmentation of steroids or pulse steroids and other immunosuppressive drugs for treatment of transplant graft rejection. Immunosuppressive regimens including cyclosporine for organ transplant recipients have been reported to have a decreased incidence of hyperinfection *Strongyloides*. This has been attributed to the anti-helminthic properties cyclosporine demonstrated in mouse models.[5] Organ transplant recipients can develop hyperinfection syndrome from endogeneous reactivation and by acquisition of *Strongyloides* from the transplanted organ and obligatory immunosuppression.[6]

The diagnosis of *Strongyloides* hyperinfection syndrome requires physician awareness of this infection and the clinical setting in which it occurs. There are several clues to the diagnosis:

1. Eosinophilia may be modest or absent. It may be marginal and transient so that it is not recognized. Systemic steroids and host debilitation may suppress this characteristic finding. The presence of eosinophilia should initiate a vigorous search for parasites.
2. Unexplained or persistent bacteremia with enteric organisms despite administration of appropriate antibiotics; gram negative or polymicrobial sepsis.
3. Serious infection (pneumonia, meningitis or bacteremia) from a suspected intraabdominal source. Gram negative bacteria follow the parasite through the intestinal wall or piggyback on the larvae. These bacteria produce the peculiar winding trails or serpiginous tracks on blood agar plates from culture of a body fluid with *Strongyloides* larvae.[7,8]
4. Nonspecific gastrointestinal symptoms (abdominal pain and distention, diarrhea, nausea and vomiting, constipation, gastrointestinal [GI] bleeding, or ulceration). The clinical picture may mimic ulcerative colitis.
5. Nonspecific pulmonary symptoms and signs (cough, wheezing, hemoptysis [massive in some cases], transient interstitial infiltrates); severe pulmonary disease and acute respiratory distress syndrome (ARDS).
6. Concurrent infection or prior therapy for other intestinal parasites.

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7. History of residence or travel to an endemic area even many years previously.

In any of these clinical settings, the thumbprint sign of periumbilical purpura is pathognomonic of hyperinfection *Strongyloides*.[9,10] Most of the multiple purpuric lesions appear as small ecchymoses, as if caused by the pressure of thumbs or other fingers during physical examination of the abdomen. The purpura radiates from the umbilicus and progresses to involve the flanks and proximal lower extremities. Innumerable fine petechiae rapidly develop over 24–48 h as a reticulated pattern of linear and serpiginous purpuric streaks.[11,12]

The vascular distribution of the lesions of hyperinfection *Strongyloides* closely parallels that of the caput medusa seen in chronic liver disease with portal hypertension. In that setting, increased portal pressure leads to retrograde flow through the periumbilical portosystemic anastomoses. The patients reported with periumbilical purpura had been placed on respirators before the development of their skin lesions. Positive pressure ventilation produces a rise in portal pressure. It is hypothesized that numerous larvae leave the host's bowel through the superior and inferior mesenteric veins entering the liver. Patients receiving respiratory assistance have transient rises in portal pressure, shunting portal blood through the periumbilical portal systemic shunt. This blood carries numerous larvae that, on reaching the dermal vascular plexus, cause extravasation of red blood cells.[9] A subtle case of two faint periumbilical purpuric patches was seen by one of the authors in a patient with mild gastrointestinal and pulmonary symptoms who was not on mechanical ventilation. Skin biopsy revealed the filariform larvae of *Strongyloides* supporting the hypothesis that while the larvae may migrate through the skin during hyperinfection, positive pressure mechanical ventilation is required to produce the classically described periumbilical thumbprint purpura. A 25-year-old Mexican man with acquired immune deficiency syndrome (AIDS) (CD4 count 70) was hospitalized with GI complaints, weight loss, and numerous 2–3 mm purpuric papules on his abdomen. Skin biopsy demonstrated filariform larvae of *Strongyloides*.[13]

Strongyloides hyperinfection syndrome can be confirmed by microscopic examination of the nasogastric aspirates, bronchopulmonary lavage specimens, or skin biopsy. The filariform larvae are immediately infective, so gloves must be worn when handling these specimens to prevent the larvae from entering mucocutaneous surfaces of the health care worker. The skin biopsy from a purpuric patch readily demonstrates *Strongyloides* filariform larvae in and around blood vessels and throughout the dermis in association with extravasated red blood cells. Multiple longitudinal and cross-sections of the larvae are usually seen. There is a significant absence of any inflammatory cell infiltrate. Serologic tests are useful in patients with negative stool exams but may not be reliable for immunocompromised hosts.[7]

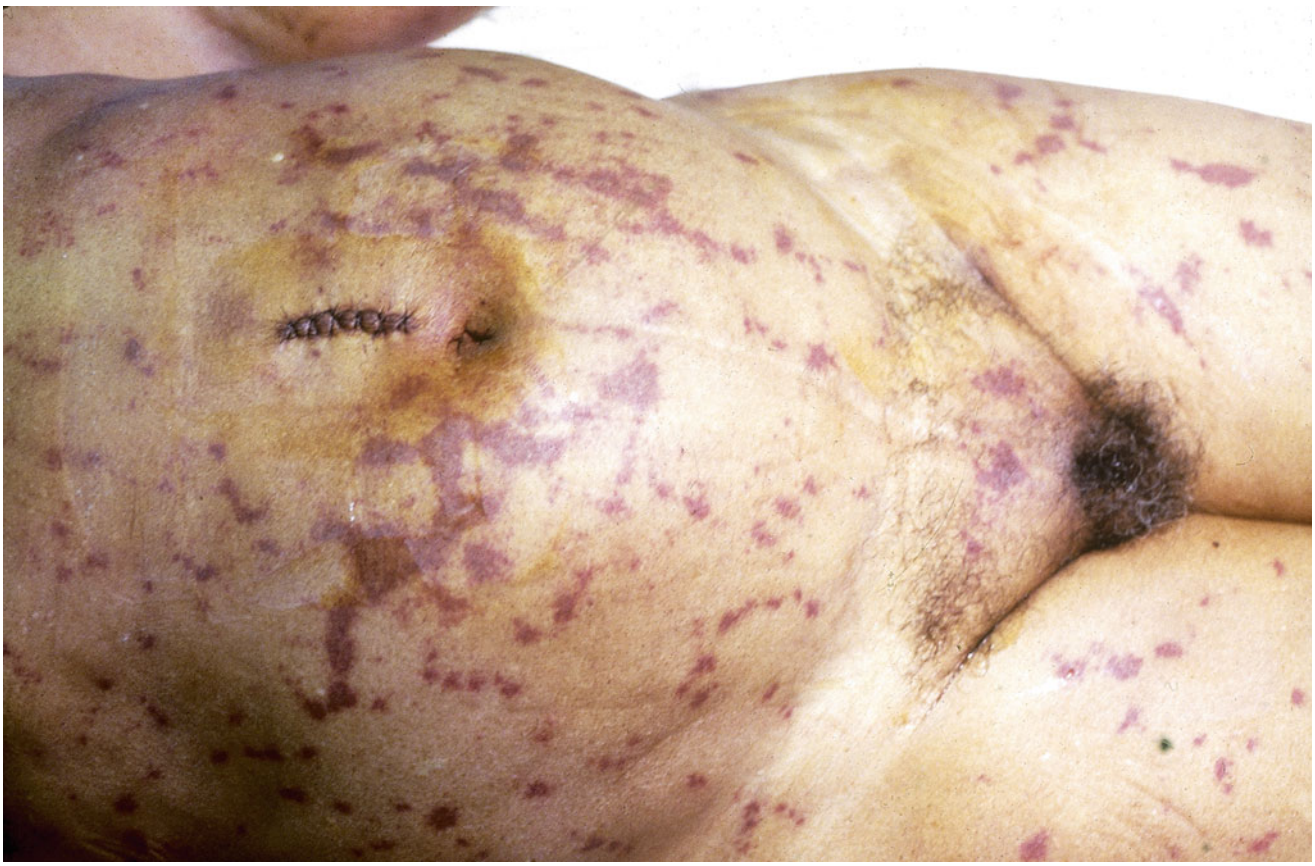

Figure 10.1. A 62-year-old woman with polymyositis on systemic steroids was from the Dominican Republic and had lived in the USA for 10 years. She presented with fever, abdominal pain, and bilateral interstitial pulmonary infiltrates. Nonpalpable periumbilical purpura appeared 24 h after a normal exploratory laparotomy

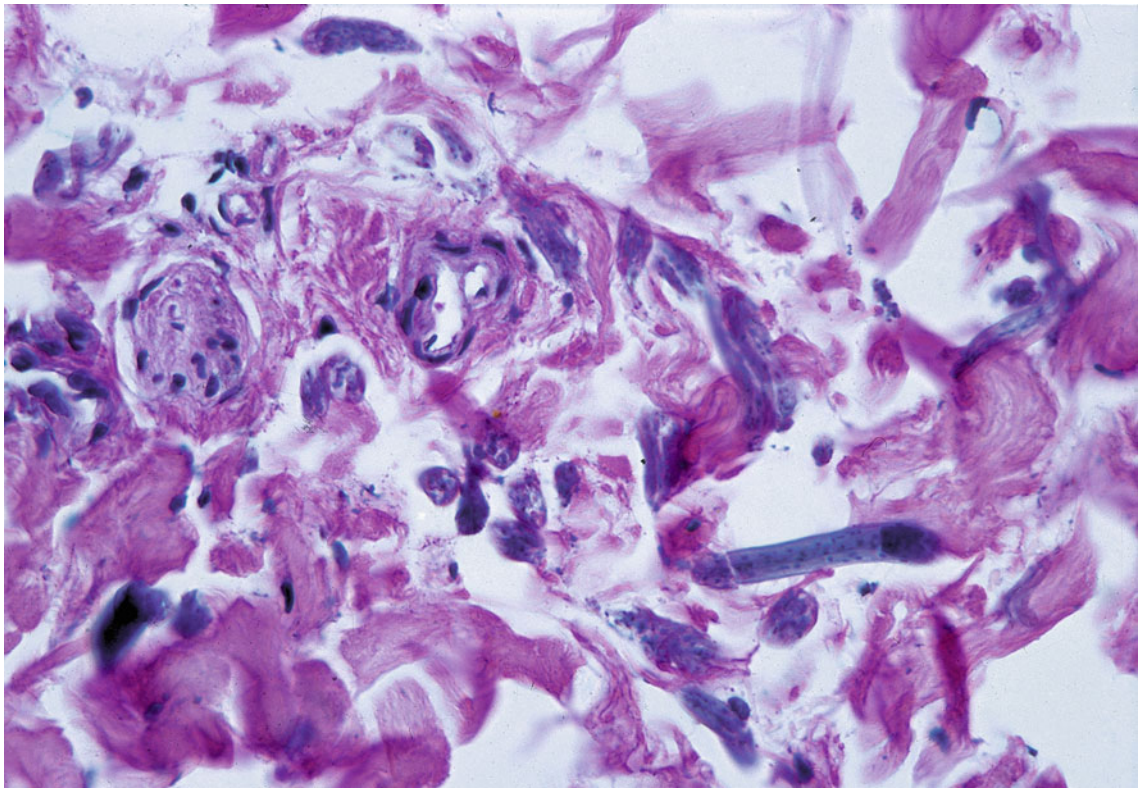

Figure 10.2. Skin biopsy of the purpura showed multiple longitudinal and cross sections of the larvae of *Strongyloides*. There was a significant absence of an inflammatory response to the larvae, which accounted for the eruption being nonpalpable

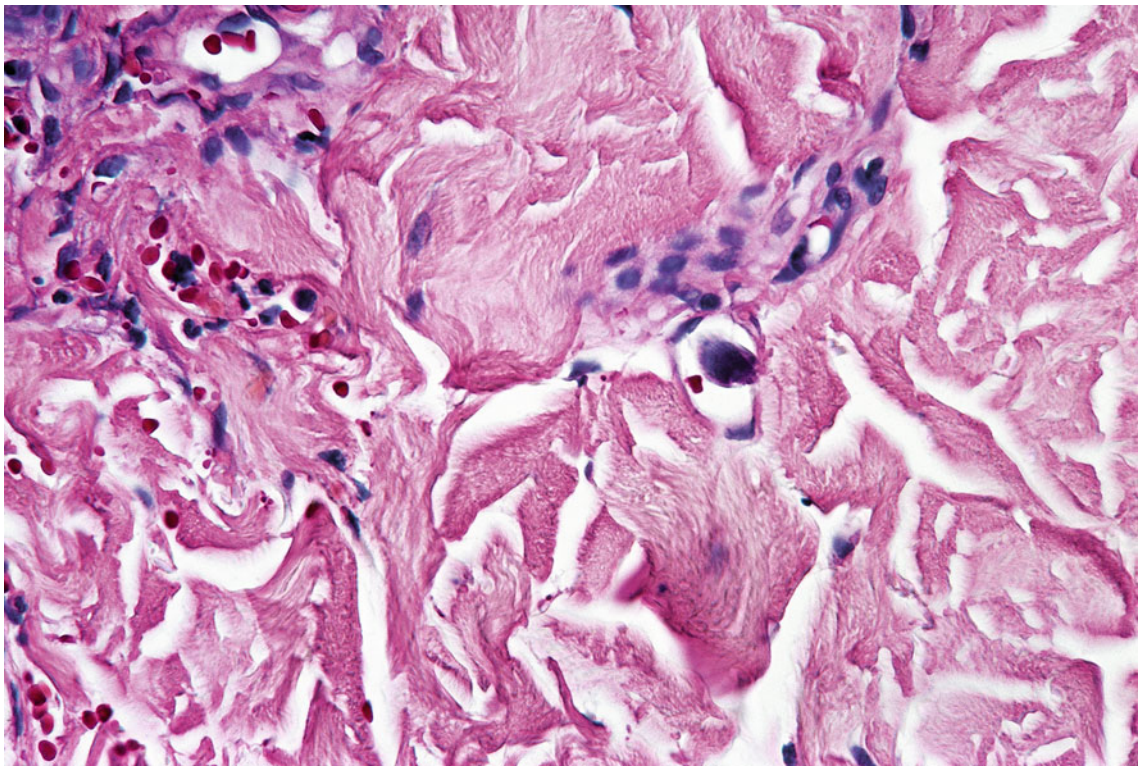

Figure 10.3. Skin biopsy with intravascular larvae of *Strongyloides* without an inflammatory response

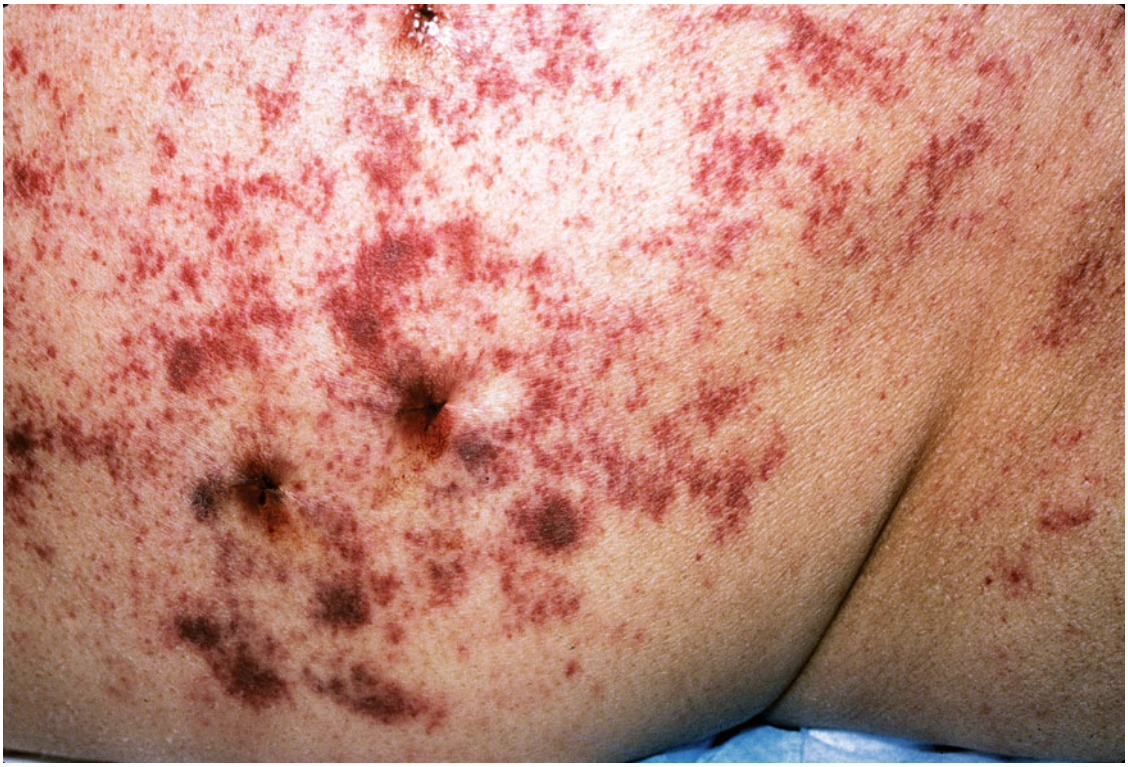

Figure 10.4. A 60-year-old man, born in Ecuador, had been treated for 7 years for asthma with many courses of systemic steroids. Blood eosinophilia was often greater than 15% and attributed to asthma after a negative stool for ova and parasites. On his last hospital admission because of respiratory distress he was intubated. Less than 12 h later he developed periumbilical purpura

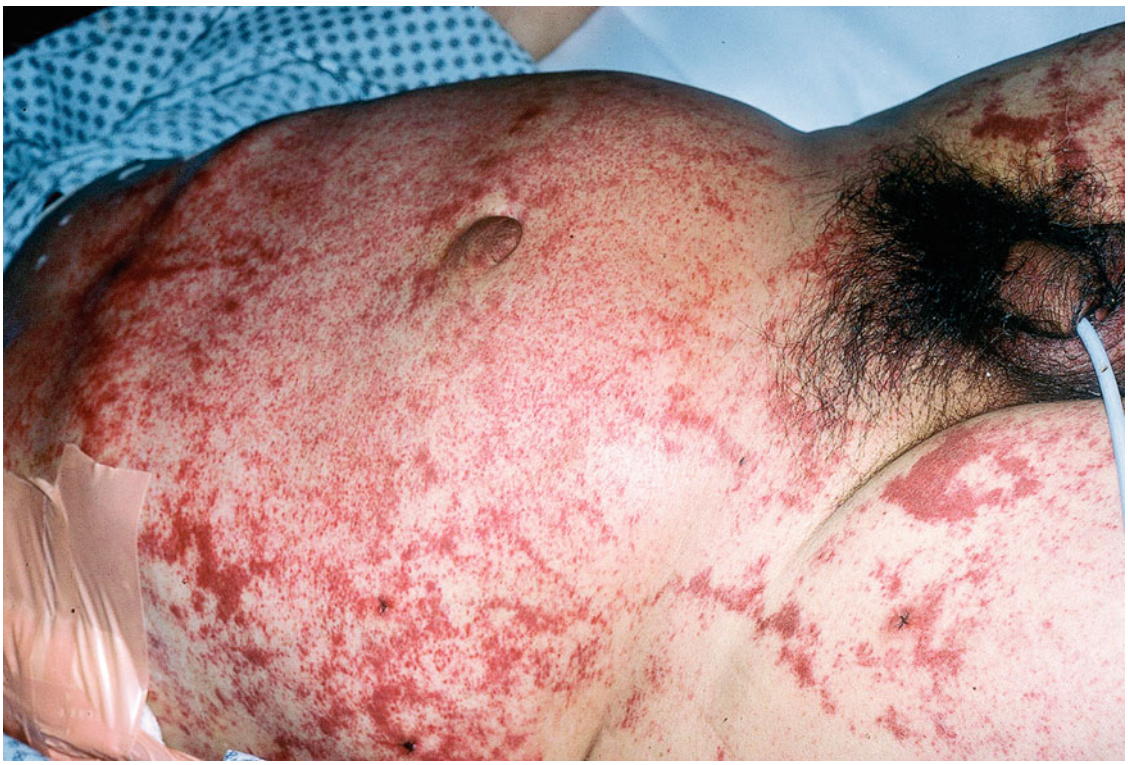

Figure 10.5. Multiple purpuric thumbprints appeared on the abdomen, flanks, and proximal thighs

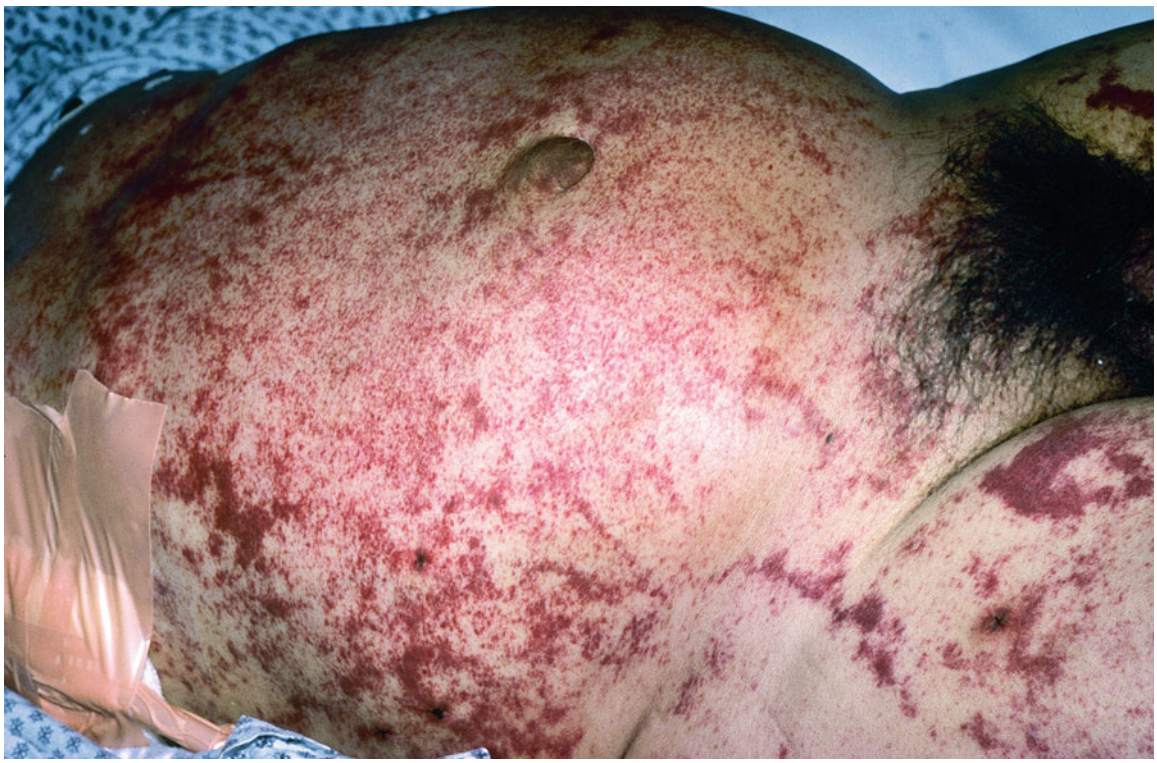

Figure 10.6. Over the next 24 h, innumerable petechiae developed in the same areas. Skin biopsy of purpura demonstrated larvae throughout the dermis both inside and outside of blood vessels

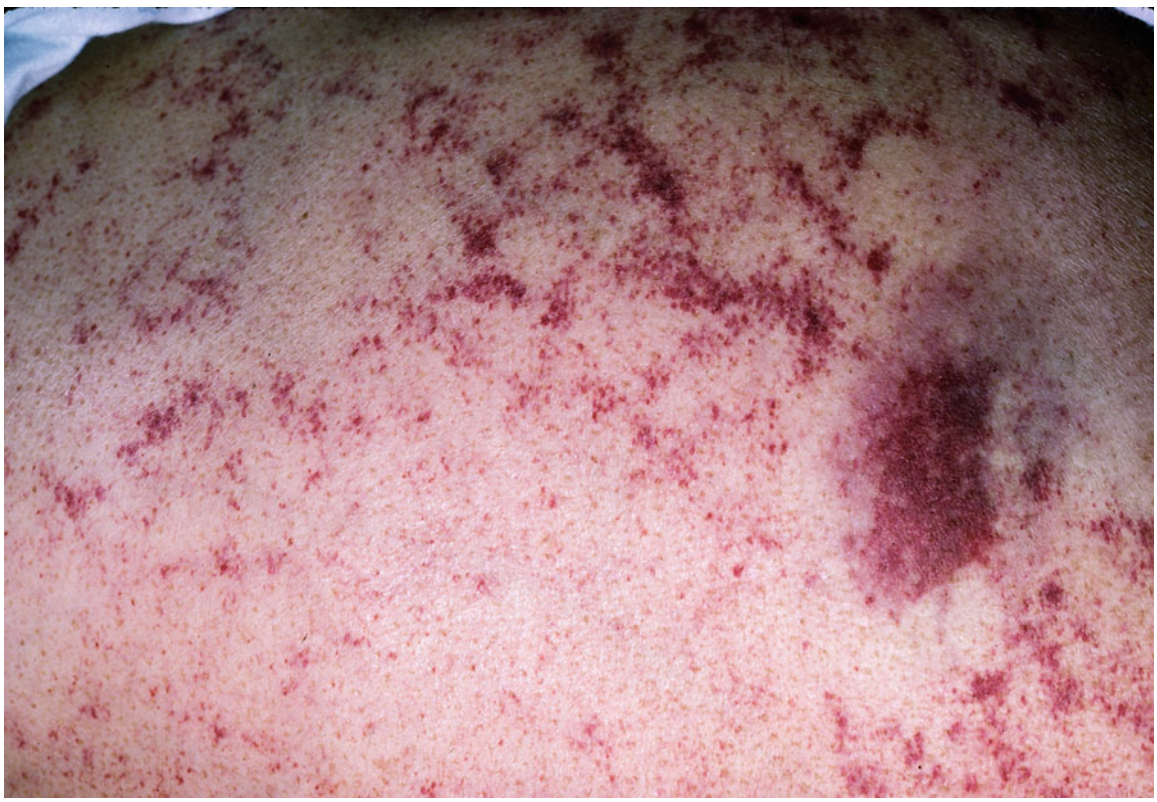

Figure 10.7. Close-up of the purpuric macules on the flank of the same patient shown in Figs. 10.3–10.6

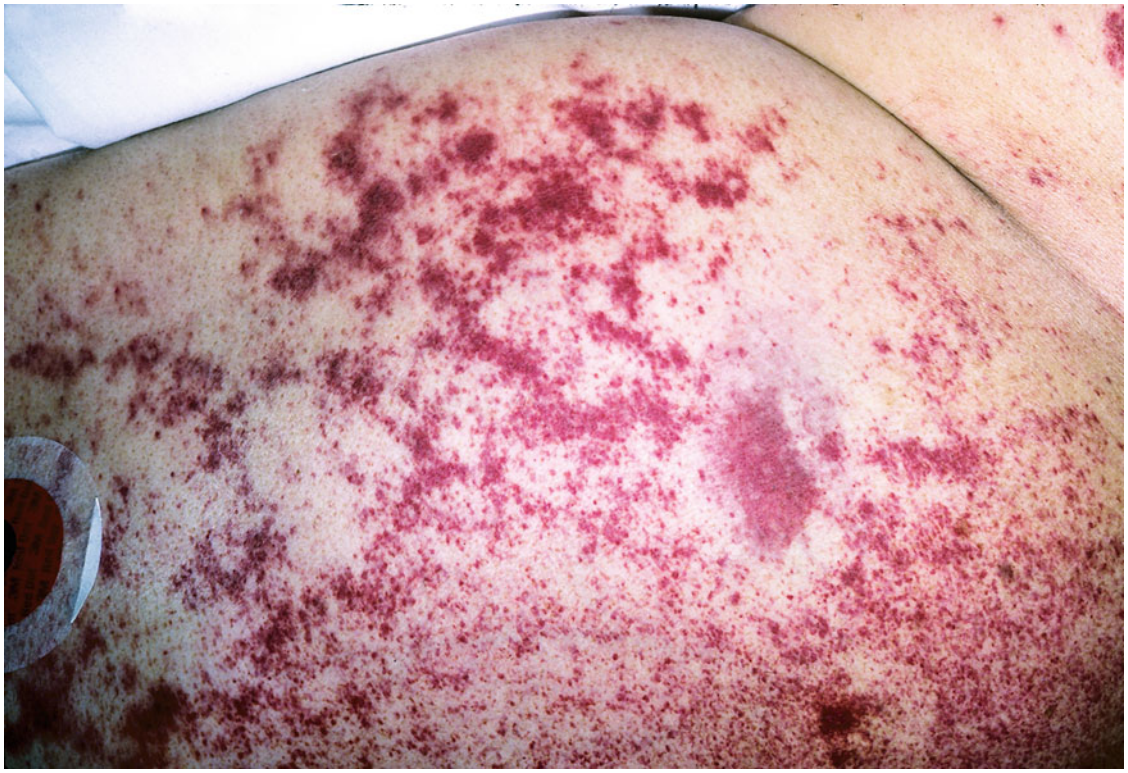

Figure 10.8. Within 48 h, the purpuric macules spread into a vascular network-like pattern with a multitude of petechiae

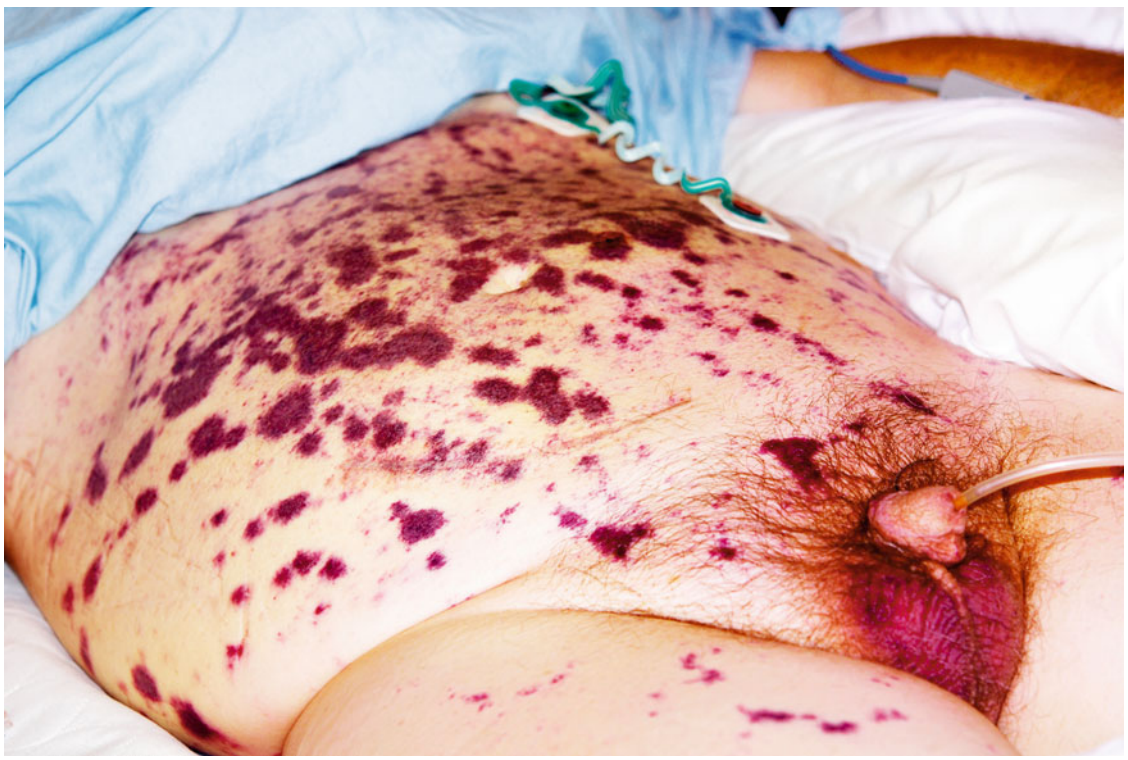

Figure 10.9. A 67-year-old man with a history of renal transplantation with a linear array thumbprint purpura from hyperinfection *Strongyloides*. The organism was acquired from the donor transplanted kidney. Bronchial washings, gastrointestinal aspirates, and skin biopsy were positive for *Strongyloides*

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