15.1 Introduction

Subcutaneous extravasation is a well-recognized complication of intravenous administration of iodinated contrast media (Cohan et al. 1996; Federle et al. 1998; Cochrane et al. 2001; Pond and Dorr 1993; Runge et al. 2002; Wang et al. 2007). The incidence of extravasation after mechanical bolus injection is higher than that reported for hand-injection or drip-infusion techniques, but there seems to be no relation between injection rate and extravasation frequency (Pond and Dorr 1993; Jacobs et al. 1998). The clinical presentation is variable. Most extravasations involve small volumes of contrast material and induce minimal swelling or localized erythema, which diminish rapidly. Pain is the most common subjective symptom (Wang et al. 2007). Extensive tissue necrosis and severe skin and subcutaneous ulcerations are rare and usually follow high-volume extravasations (Cohan et al. 1996; Ayre-Smith 1982).

15.2 Risk Factors

15.2.1 Patient Factors

Infants, small children and unconscious patients are more likely to develop extravasation (Cohan et al. 1996) because they are unable to complain of pain at the injection site. Patients undergoing chemotherapy are also at a higher risk because chemotherapy may induce fragility of the wall of the vein. Extravasation injuries are also more severe in patients with low muscular mass and atrophic subcutaneous tissue. In addition, patients with arterial insufficiency (e.g. atherosclerosis, diabetes mellitus or connective tissue diseases) or compromised venous (e.g. thrombosis) or lymphatic drainage (e.g. radiation therapy, surgery or regional node dissection) are less able to tolerate extravasation than those with unimpaired circulation.
15.2.2 Contrast Media Type and Volume

Extravasation of low-osmolar contrast media is better tolerated than extravasation of high-osmolar media. The osmolality threshold for significant tissue injury is estimated to be 1.025–1.420 mOsm kg⁻¹ water (Cohan et al. 1990a; Elam et al. 1991; Sistrom et al. 1991). However, five severe injuries have been reported with nonionic contrast media, one of them in a 22-month-old child. None of them required reconstructive surgery (Pond et al. 1992; Young 1994; Memolo et al. 1993; Benson et al. 1996; Wang et al. 2007).

Runge et al. (2002) showed, after extravascular injection of 0.3 mL of MR contrast medium in the hind limb of rats, that in particular the higher osmolar agents like gadopentetate dimeglumine and gadoversetamide have more harmful consequences than agents with a lower osmolality such as gadodiamide and gadoteridol.

The vast majority of extravasations involve small volumes of contrast material and symptoms resolve completely within 24 h (Cohan et al. 1996, 1997; Federle et al. 1998; Jacobs et al. 1998; Sistrom et al. 1991). Severe skin ulceration and necrosis have been seen after extravasation of volumes as small as 10 mL, but that is very rare (Ayre-Smith 1982). Large-volume extravasation may lead to severe damage to extravascular tissue and is most likely to occur when contrast medium is injected with an automated power injector and the injection site is not closely monitored (Cohan et al. 1996, 1997).

15.2.3 Factors due to Injection Technique

The type of venous access affects the frequency of extravasation. In 40% of one series of patients with contrast medium extravasation, indwelling intravenous lines were used (Sistrom et al. 1991). Extravasations are more frequent with metallic needles than with plastic cannulae (Gothlin 1972). The site of injection appears to be important. Seventy-eight percent of 36 patients who had contrast medium injected through a dorsal vein of the great toe for lower limb phlebography developed extravasation (Gothlin 1972). The use of tourniquets and the presence of oedema also increase the risk of extravasation with lower limb phlebography (Cohan et al. 1996). Injections into the dorsum of the hand are also frequently associated with extravasation injury (Gault 1993).

Mechanical power injection for CT studies is responsible for many extravasation injuries. The frequency of extravasation with power injection rates between 1 and 2 mL s⁻¹ varies from 0.2 to 0.4% (Federle et al. 1998; Cohan et al. 1990a; Sistrom et al. 1991; Miles et al. 1990; Kaste and Young 1996). In a large study where injection rate was accounted for in 421 patients having extravasation, 27% were injected at the rate of less than 2 mL s⁻¹, 50% at 2–3 mL s⁻¹, and 23% at more than 3 mL s⁻¹ (Wang et al. 2007).

In a study by Jacobs et al. (1998), the extravasation rate (0.6%) did not differ significantly between groups of patients receiving different injection rates of contrast media. In addition, no correlation was noted between the extravasation rate and catheter location, catheter size and catheter type. High-volume extravasation may occur if the extravasation is deep or if the patient remains asymptomatic.

15.2.4 Mechanisms and Toxicity

Multiple factors are involved in the pathogenesis of extravasation injuries.

15.2.4.1 Osmolality

The first factor is osmolality above 1.025–1.420 mOsm kg⁻¹ water. Both iodinated radiographic and MR contrast agents of low osmolality are better tolerated than high-osmolar iodinated contrast agents. With MR imaging contrast agents, the osmotic loads and the volumes that are administered are markedly lower than with iodinated agents. However, in rats, extravasation of dimeglumine gadopentate (1960 mmol kg⁻¹ water) was associated with a higher incidence of necrosis, hemorrhage and edema compared to gadoteridol (789 mmol kg⁻¹ water) (Cohan et al. 1991; Runge et al. 2002). The latter, at a concentration of 0.5 mol L⁻¹, was no more toxic than 0.9% saline.

15.2.4.2 Cytotoxicity

The second factor is the cytotoxicity of the contrast media, with conflicting results in the literature when ionic and nonionic contrast media are compared. In a laboratory study (McAlister and Palmer 1971), extravasated ionic contrast media produced acute inflammation followed by a chronic inflammatory