turbinates and especially the inferior turbinates suggest that the drug was moving from the frontal cavity over the turbinates and then being cleared toward the throat. This would also be expected due to the normal mucociliary clearance mechanisms, which are known to not be affected by the drug. This motion, suggested by the data curves, was clearly visible in time-lapse video display of the data. The frontal cavity may be serving as a reservoir of drug to replenish that being eliminated from the turbinates. The superior turbinates received about half the total dose of the inferior turbinates and also exhibited more pronounced individual variation in curve shape during the first 10 min after inhalation. Those variations correlated (inversely) with changes in the frontal cavity uptake. Individual differences strongly diminished after the first 10 min. Other clear conclusions from the data are that the amount of drug in the target areas remains significant at 1.5 hr postadministration and that the clearance rates (Table 1) suggest that the drug will persist in those areas. This is an important observation in light of the fact that the target areas are well perfused, so a drug that was readily dissolved and absorbed into the tissues could be rapidly removed. The observation period was limited by the half-life of the ^{11}C label, so it is difficult to estimate and extrapolate the slow washout or absorption component of the curves. Still, simple linear or exponential extrapolations predict that microgram amounts of drug should be present on the target tissues for at least several additional hours.

CONCLUSION

The purpose of this study was limited to demonstration of the ability of PET to provide this unique type of information and to function effectively for measurement of dose delivery and pharmacokinetics. It was not intended to address clinical use and effectiveness or to assess the delivery system. It is clear that regional biodistribution and kinetic data for the active ingredient in the drug formulation could not be determined by other means. This direct in vivo evaluation of the formulation in only three volunteers is a more reliable indicator of its performance than inferences drawn even from extensive in vitro experiments. Despite the small sample size and expected intersubject variations, the study shows effective deposition of drug into the target tissues and demonstrates that the clearance of drug from the target areas is slow enough to allow significant amounts of drug to be present for at least several hours. This information was not otherwise available to the manufacturer of the formulation. Although penetration of drug into the sinus cavities was not expected, it has now been demonstrated and measured. We believe that this study clearly demonstrates the value and effectiveness of PET for investigation and screening of locally administered drug formulations.

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Increased Subglottic Gallium Uptake in Relapsing Polychondritis

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Gallium scintigraphy was performed on a 14-yr-old girl with subglottic airway narrowing that caused wheezing and dyspnea. The study showed increased gallium uptake in the neck. A biopsy was performed on the subglottic region, and the histology was compatible with relapsing polychondritis. After treatment with steroids, laboratory data that had indicated active inflammation soon normalized. Repeat gallium scintigraphy showed diminished uptake, although the subglottic stenosis did not improve. These results suggest that gallium scintigraphy is valuable for evaluating inflammatory activity in relapsing polychondritis.

Key Words: relapsing polychondritis; gallium scintigraphy; tracheal stenosis

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Relapsing polychondritis is thought to be a rare disorder characterized by inflammation of cartilaginous structures throughout the body. Its cause is unknown but it is thought to be autoimmune mediated. The inflammatory process commonly involves the ears, eyes and joints, resulting in pain and deformity. In more than 50% of patients, the cartilages of the upper airway are affected. In such patients, the stenotic lesions can be life threatening and tracheostomy may be required. We describe gallium scintigraphy in a patient with relapsing polychondritis presenting persistent wheezing and inspiratory dyspnea.

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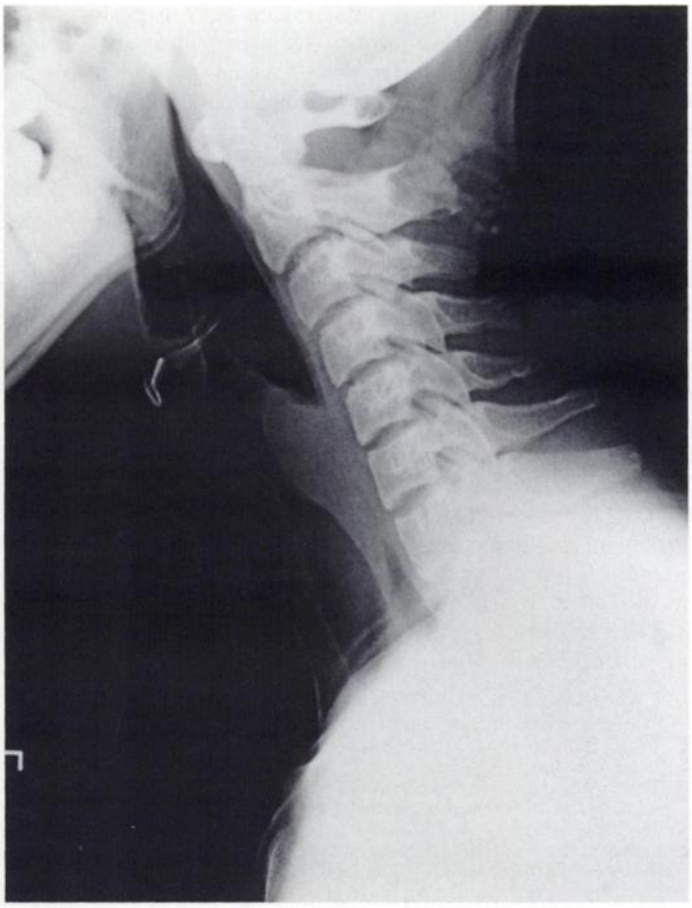

FIGURE 1. Lateral radiograph of neck shows smooth symmetrical narrowing of subglottic part of trachea.

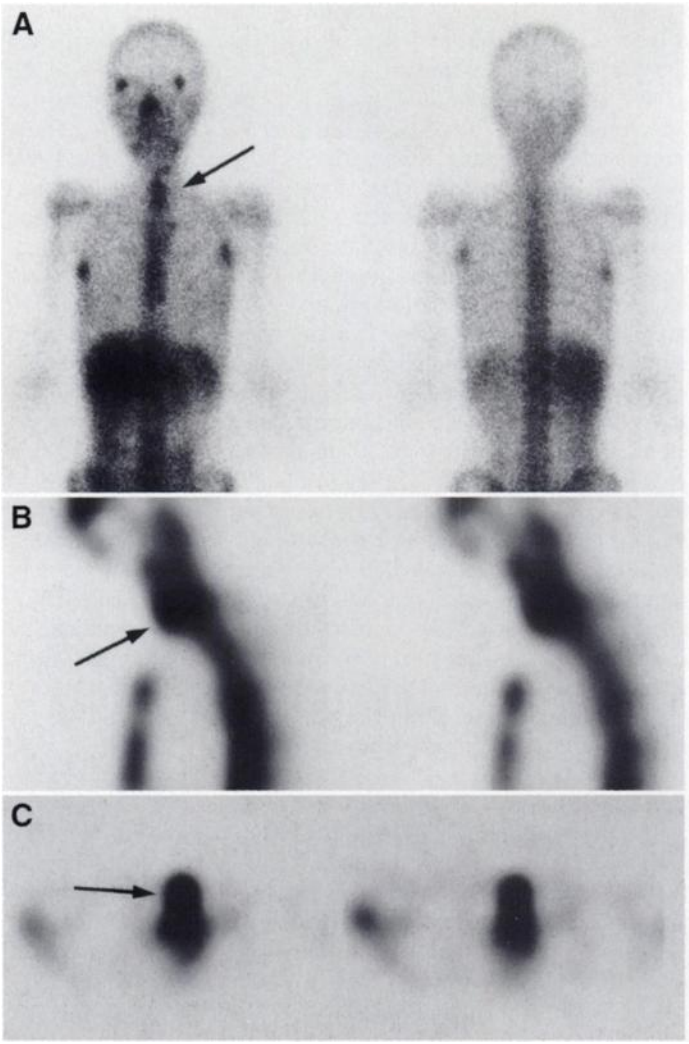

FIGURE 2. (A) Gallium scintigrams before steroid treatment demonstrate intense uptake in the medial neck and bilateral chest wall. On sagittal (B) and axial (C) SPECT images of neck, arrows show abnormal uptake anterior to the vertebral body.

CASE REPORT

A 14-yr-old girl was admitted to our hospital in January 1997, with wheezing, hoarseness and dysphagia for approximately 1 mo. Previous treatments for bronchial asthma and upper respiratory tract infection had failed to ease her symptoms. Inspiratory stridor developed, and the patient lost 7 kg in body weight in this 1 mo. In addition to these complaints, physical examination revealed a saddle nose deformity, which the patient's mother had noticed 7 or 8 yr previously. Laboratory findings revealed C-reactive protein of 6.6 mg/dl, gamma globulin of 24.0% and white blood cell count of 10,200/mm^3. Chest radiographs showed only focal callus formation on right fifth rib and left fourth rib perhaps representing fractures, and no abnormal findings were seen in lung fields or mediastinum. A noncontrast lateral radiograph (Fig. 1) and contrast and noncontrast CT scans of the neck revealed apparent annular narrowing of the subglottic larynx and upper trachea surrounded by enhanced thick soft tissue. Laryngoscopy showed subglottic smooth severe stenosis, and tracheostomy was performed. Since some kind of neoplasm was suspected because of the weight loss and soft-tissue mass, gallium scintigraphy was performed. Seventy-two hours after 72 MBq ^{67}Ga-citrate were injected intravenously, whole-body and SPECT images of the neck were obtained. Focal abnormal accumulation was seen in the medial neck and bilateral chest wall. SPECT images showed intense abnormal bandlike accumulation anterior to the uptake of cervical vertebrae, which demonstrated the subglottic lesion. The hot spots in each lateral chest wall corresponded to the rib lesions (Fig. 2). Bone scintigraphy showed no abnormal accumulation in the neck.

A biopsy of the subglottic soft-tissue wall showed loss of basophilic staining of the degenerative cartilage matrix, decreased number of chondrocytes, invasion of capillaries and mild pericapillary neutrophilic and mononuclear leukocytic infiltration. On the basis of the clinical and pathological evidence, relapsing polychondritis was diagnosed, and treatment using predonisolone was begun in February 1997.

After 1 wk, laboratory data had normalized. Four weeks after steroid therapy was begun, follow-up gallium scintigraphy was performed. No abnormal uptake was seen in the neck, and less intense accumulation than before was seen in bilateral ribs. Even on the SPECT images, abnormal accumulation in the subglottic lesion anterior to the vertebral body had disappeared (Fig. 3). However, the radiographic and laryngoscopic appearance, i.e., the stenosis of the subglottic region, remained unchanged, so permanent tracheostomy was necessary.

DISCUSSION

Relapsing polychondritis was first reported by Jaksch-Wartenhorst in 1923 (*1*). This is still believed to be a rare disorder characterized by recurrent episodes of inflammation affecting cartilaginous structures throughout the body. A diagnosis of relapsing polychondritis depends on several characteristic findings of the disease, and McAdam et al. (*2*) defined the diagnostic criteria in 1976. Histological findings show typical perichondral inflammation, loss of basophilic staining of cartilaginous matrix in the early stage and dissolution and fragmen-

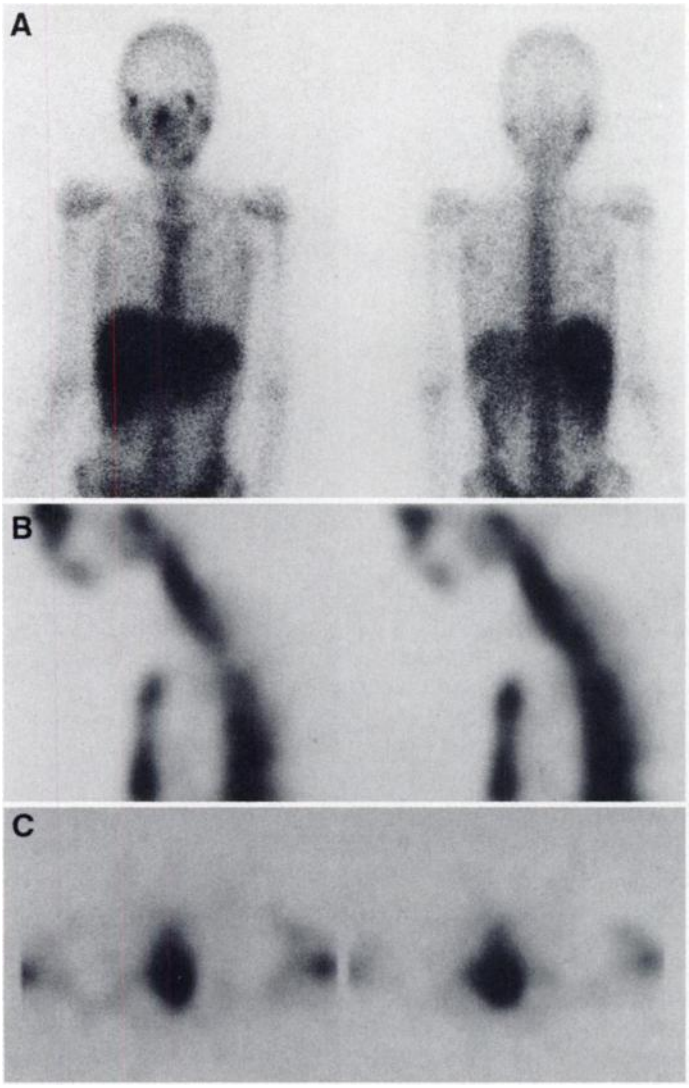

FIGURE 3. (A) Gallium scintigrams after steroid therapy show that abnormal uptake in medial neck has disappeared. At the same time, stenotic findings remained on sagittal (B) and axial (C) SPECT images.

tation of cartilaginous structures, with replacement of fibrous tissue and inflammatory changes in adjacent connective tissue (*2*).

The external ear is affected most frequently, and the nose, joints, external auditory canal, eustachian tube and other cartilage are involved less frequently (*1–3*). The airway cartilage is affected in more than half of all patients. The involvement can occur in the larynx, trachea and even bronchi, can result in collapse of tracheal rings, and can narrow the airway due to edema, large amounts of granulation tissue and fibrous scarring (*3*). Therefore, the stenosis may not always improve even after the inflammation has been suppressed, although Im et al. (*4*) reported two patients in whom tracheobronchial wall thickening was decreased after treatment. The stenotic change of the airway often brings about choking and recurrent pneumonia that may cause death. Therefore, estimating whether the inflammation is active is important for appropriate treatment to prevent the progression of the disease (*3–5*). To date, laboratory data, symptoms and radiographic findings have been used to assess this disorder (*2–7*). In particular, objective assessment of abnormalities of airway was made on noncontrast radiographs or CT scans (*8*). It has been reported that plain chest radiographs can indicate two thirds of the abnormalities involving the trachea or main bronchi and that CT detects 91%–97% of abnormalities (*9*). By its nature, this disorder is characterized by an episodic course with exacerbations and remission of inflammation on one hand. Permanent deformity can be caused by only one episode of inflammation, on the other hand. This patient showed that after treatment there may be a dissociation between the radiographic findings and the activity of inflammation that C-reactive protein, white blood cell count and gallium-citrate uptake made clear. Thus, the findings of radiography, CT and even laryngoscopy might not always demonstrate the actual inflammatory activity. We could not follow the histological difference between before and after treatment, but we theorize that steroid therapy sedated only the infiltration of the leukocytes without removing the scar, which caused narrowing of the airway.

Many authors have reported on ways to diagnose or treat this disorder (*6,8,10,11*). Gallium scintigraphy has little diagnostic value when a biopsy is performed. The way to monitor the response to therapy has not been discussed in depth. Laboratory data, which are usually used for monitoring, might reflect the inflammatory activity of other noncritical lesions. As demonstrated in this patient, radiographic findings cannot always reflect the real activity. Güngor et al. (*12*) reported the usefulness of methylene diphosphonate bone scintigraphy in follow-up of costochondral junctional lesions. We support the usefulness of bone scintigraphy for the lesion adjacent to bone, but it is not sufficient to examine lesions unrelated to bone, for example, ears, trachea and bronchi.

CONCLUSION

In this patient, gallium scintigraphy was superior to radiographic and laryngoscopic findings in estimating the activity of inflammation. This case suggested that in patients with dreadful tracheal lesions, taking into account the characteristics and natural course of the disease, gallium scintigraphy may be useful in assessing focal inflammatory activity.

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