tion to a more aggressive disorder like Richter's syndrome. In the only other reported case of cord compression caused by CLL the disease was also in the early stages at the time of this complication but the symptoms developed rather slowly—over three months.³ In both these cases the lesion was extradural, which is typical of a metastatic tumour.⁴

There have been several other reports of patients who had a more diffuse central nervous system disease as a result of blast cell infiltration of the brain or spinal cord.^{2,5-8} These patients had various symptoms like dementia, coma, and cerebral nerve palsy but no localised deposits. Post mortem examination in one series showed central nervous system infiltration by blast cells in 10 out of 14 cases of advanced CLL, though none of these patients had any neurological symptoms.⁹ The predominant lesion in one case of spinal cord disease was perivascular infiltration.⁸

Though cord compression is a very rare complication of CLL, it is potentially treatable and early diagnosis provides the best chance for

the patient. Our patient showed surgically satisfactory improvement after surgical decompression followed by local radiotherapy. In the other reported case such measures could not be taken because of the delay in the diagnosis and because the disease rapidly proved fatal.³

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Thorotrast granuloma: an unexpected diagnosis

S V Polaczar, R W Laing, R Loomes

Abstract

An example of a Thorotrast granuloma (thorotrastoma) occurred in the neck of a patient 44 years after a carotid angiogram in which Thorotrast was used as radiological contrast medium. The lesion had produced a "cold" abscess and the patient was undergoing treatment for retropharyngeal tuberculosis. Thorotrast leakage can produce unusual clinical symptoms and signs which are frequently misdiagnosed.

Between 1930 and 1950 as many as 100 000 people were subjected to a large variety of radiological studies using the contrast medium Thorotrast,¹ a colloidal suspension of radioactive thorium dioxide in a dextran medium. Due to its high density Thorotrast is well suited to its role as a radiological contrast medium, and was widely used in intravascular studies, particularly carotid angiography, and as luminal contrast in hollow body cavities, such as bladder and bronchus. Because Thorotrast is removed from the general circulation by reticuloendothelial macrophages, and hence concentrated in the liver, spleen and bone marrow, it was also used in radiological visualisation of these organs.

Thorotrast is, however, highly radioactive with predominant α emission and a half-life of 1.39×10^{10} years. Excretion of ²³²thorium is negligible, and thus the body becomes the permanent site of deposition of this radioactive and potentially hazardous material. In spite of an increasing realisation of its carcinogenic potential² Thorotrast continued to be used widely in many countries, including the United Kingdom until the early 1950s.

Case report

A 66 year old man presented with a five week history of non-productive cough, sore throat, and severe pain in the right side of the neck and right occiput, with restricted neck movements and some dysphagia. He was treated, initially by his general practitioner, with antibiotics to no avail.

On subsequent examination in the ear, nose, and throat outpatients clinic the posterior pharyngeal wall on the right side was noted to be swollen with adherent inflammatory slough, and there was some induration of the right side of the neck. The palate was mobile and no abnormalities were detected in the nasal passages. Some fasciculation of the right side of the tongue was noted. Small lymph nodes were

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palpable in the right supraclavicular fossa and in the upper right jugular chain. The patient had a temperature of 37.5°C and a tachycardia of 120 beats/minute. A right lateral neck x ray picture showed a diffuse retropharyngeal mass with spotty calcification which was reported as being strongly suspicious of retropharyngeal tuberculosis.

Examination of the postnasal space was performed under general anaesthetic and a large area of ulceration was seen extending from the level of the palate along the posterior pharyngeal wall. Focal tissue calcification was also noted.

A biopsy specimen taken at this time showed largely non-specific inflammatory changes, but of particular interest was the inclusion of a necrotic fragment of tissue showing focal microcalcification and the presence of abundant granular material. The latter appeared a light brown colour in the haematoxylin and eosin preparation. The possibility that this might be caused by iron or melanin pigment was excluded by the appropriate histochemical stains.

Analysis of this material by the technique of x ray energy dispersal (EDAX) showed a strong Thorium peak. This was confirmed by subsequent slide autoradiography in which radioactive α emissions were conspicuous (figure). The patient was further questioned and found to have undergone carotid angiography 44 years previously for assessment of a right ophthalmic arterial thrombosis. Ten years before presentation a spermatocytic seminoma had also been removed from the left testis.

Thorium measurements, performed by the department of medical physics, detected 576 mg $^{232}\text{thorium}$ in the posterior nasal space and 135 mg in the liver. Tumour tissue blocks of the testicular seminoma were also examined and found to contain 1–2 mg. The patient was treated conservatively with further antibiotics and a liquid diet. The area of ulceration was

slow to resolve but had finally healed five months later.

Discussion

Late complications of Thorotrast administration were initially suspected from animal studies.² Two recognised principal late effects are malignancy and fibrosis local to the site of Thorotrast injection. The first human malignancy attributed to Thorotrast was reported in the liver,³ and hepatic angiosarcoma and cholangiocarcinoma are now recognised as the most common malignancies associated with Thorotrast use. Malignant tumours usually develop after a latency of 12–45 years.⁴

In addition to malignancy of the reticulo-endothelial system, principally the liver, two further categories of malignancy attributable to Thorotrast have been reported. First those malignancies local to the site of previous injection, including those which result from extravasation of contrast from vascular puncture. These are usually soft tissue sarcomas, although osseous and cartilaginous sarcomas have also been reported.⁵ Second, malignancy following Thorotrast retention in hollow body cavities is also recognised, these include carcinomas following pyelography, bronchography, dacrocystography and tumours of the maxillary sinus.

Testicular seminoma has not previously been reported in those patients exposed to Thorotrast. Although its occurrence in our case may be coincidental, the presence of demonstrable $^{232}\text{thorium}$ in tumour tissue suggests that Thorotrast may have played an aetiological part in the development of the tumour. Compared with the Thorotrast load to the nasopharynx and liver, thorium exposure to the testis was relatively slight, but germ cells are likely to be more sensitive to such exposure and this may account for the subsequent development of tumour at this site.

The fibrogenic effect of Thorotrast is thought to be a consequence of contrast extravasation following intravascular or intraluminal administration. Thorotrast carotid angiography produced extravasation in 3–10% of cases, and when this occurred at least 50% of patients subsequently developed a severe desmoplastic reaction to Thorotrast, producing a hard tumorous mass (thorotrast granuloma or thorotrastoma).⁶ These lesions may slowly enlarge with time and often compromise the function of entrapped nerves, blood vessels, and muscles. Weakness may develop in glossopharyngeal, vagus, spinal accessory or hypoglossal nerves (producing tongue fasciculation, evident in our patient), and in the sympathetic trunk. Severe desmoplasia may also produce progressive obliteration of the carotid and subclavian arteries or occasional lethal vascular erosion and haemorrhage. Postnasal and oropharyngeal ulceration, as occurred in this case, is a rare complication of a Thorotrast granuloma, and is thought to be a manifestation of cicatricial fibrosis compromising local vascular supply and not due to tissue damage caused by radiation.⁷

Slide autoradiogram showing granular thorium deposit (▲) and α tracks as revealed in photographic emulsion (⇧).

Most agree that conservative management of Thorotrast granulomas is appropriate.⁸ Poor healing at the biopsy site is often noted, and although healing was slow in our patient, satisfactory results were eventually obtained.

Radical neck surgery is advocated by some in an attempt to eradicate all local Thorium deposits, this has the disadvantage of a high incidence of fistula formation and does not reduce the risk of reticuloendothelial malignancy.⁸

Our patient seems to have had adequate treatment, and two years after this most recent presentation remained both locally free of tumour, and with no evidence of malignancy elsewhere.

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Synchronous squamous and glandular neoplasia of the anal canal

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Abstract

A 48 year old man presented with invasive adenocarcinoma in the wall of a non-healing anal fistula. The subsequent abdomino-perineal resection specimen showed residual invasive carcinoma coexisting with in situ carcinoma of anal glands as well as in situ squamous carcinoma of the anal canal. The epithelium of the anal canal had koilocytotic features. DNA hybridisation studies by the dot blot technique showed weak positivity for human papillomavirus (HPV) subtypes 16, 18.

This case illustrates a number of important points—namely, anal fistulas, particularly non-healing fistulas should be biopsied to exclude malignancy; some adenocarcinomas of the anal arise in anal glands; the coexistence of glandular and squamous carcinoma with evidence of HPV infection is highly reminiscent of similar synchronous lesions of the uterine cervix and suggests that HPV may have an aetiological role in both squamous and glandular carcinomas of the anal canal.

The anal canal is regarded as extending from the upper border of the internal sphincter to the lower border of the external sphincter and is lined by three types of epithelium. The upper third is lined by colorectal mucosa while

squamous epithelium lines the distal third and is continuous with anal skin. The middle zone may be lined by squamous, columnar, or transitional epithelium which is stratified with columnar or polygonal cells superficially. Malignant tumours of the anal canal are rare. Among these squamous cell carcinoma is the most common, some of these arising in the epithelium of the transitional zone, although some may originate in the distal anus.¹ There is an increasing incidence of squamous carcinoma of the anal canal, particularly among young men, with a known association of this carcinoma with human papillomavirus (HPV) infection.² Rarer still is the adenocarcinoma of the anal canal, the origin of which is often debated.

This is a report of a patient with, uniquely, an invasive adenocarcinoma occurring at the same time as in situ glandular and squamous cell carcinoma of the anal canal, which may shed light on the origin and pathogenesis of these tumours.

Case report

A 48 year old previously well, married man presented with an anal fistula which failed to heal despite initial surgery. With further surgery and a wedge biopsy of the wall of the fistula, an invasive adenocarcinoma was found. The patient then had an abdominoperineal resection from which he made an uneventful recovery.

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