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Case Report

Remote arterial vasculitis as a possible complication of Phosphorus-32 Radiosynovectomy

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ABSTRACT

Patients with hemophilia suffer from repeated episodes of hemarthrosis leading to chronic inflammation and synovitis. Radiosynovectomy is an effective nonsurgical modality that can reduce inflammation, pain, and hemarthrosis in such cases. We describe an adolescent male with severe Hemophilia A, who developed arterial vasculitis and perivasculitis targeting the brachiocephalic, right common carotid, and right subclabvian arteries occurring within few days after difficult Phosphorus-32 radiosynovectomy, possibly as a complication of the procedure. Despite prophylaxis with recombinant FVIII therapy, he developed chronic synovitis and underwent radionuclide synovectomy with P-32 injection to the left ankle and right knee. Five days later, he developed pain in the lower right neck and right upper chest. Computed tomography and magnetic resonance imaging and angiography demonstrated inflammation involving the arteries of the right thoracic inlet. Geiger-Mueller meter indicated increased radioactivity not only in the left ankle and right knee but also in the right upper chest. Detection of radioisotope at the right thoracic inlet corresponding to the area of vasculitis was indicative of likely deposition of the P-32 isotope in an area exposed to maximum cardiac output and increased blood flow, leading to subclavian, carotid, and innominate arteritis with surrounding edema.

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Rachel Gallant MD and Rene McNall MD declare that they have no conflict of interest. Dr. Osman Khan has served in an advisory capacity to coagulation factor manufacturing pharmaceutical companies, including Shire, Bayer, Octapharma, and Pfizer.

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Introduction

Hemophilia A and B are X-linked bleeding disorders resulting from deficiency of clotting factors VIII or IX, respectively, with severe hemophilia characterized by a factor level less than 1%. Patients in this population may develop hemarthrosis secondary to minor trauma or even normal daily activity. The inflammatory response to blood in the synovium leads to synovial hypertrophy; in turn, the thickened synovium becomes more vascular and friable, and therefore more likely to rebleed [1]. This leads to irreversible degenerative changes within the joint, which is the largest cause of morbidity in these patients. Radiosynovectomy is a nonoperative treatment modality that has been shown to reduce recurrent hemorrhage, slow progression of further joint damage, improve mobility, and reduce pain by inducing thinning and fibrosis of the synovium [2,3].

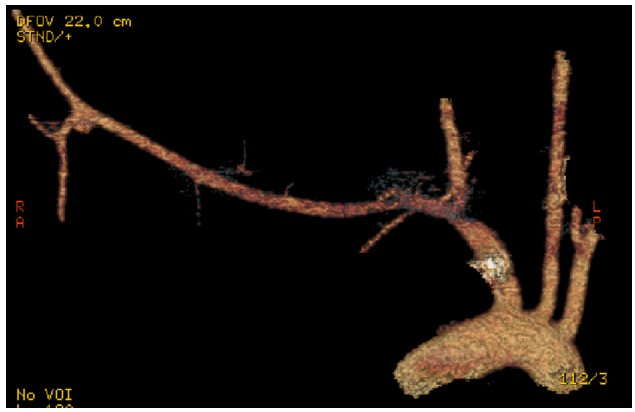

Fig. 1 – CT angiogram reveals inflammatory changes of the arteries in the right thoracic inlet concerning for infectious vs inflammatory arteritis.

Case report

We present the case of a 17-year-old boy with severe Hemophilia A, who despite his treatment with prophylactic recombinant Factor VIII 30 unit/kg every other day, developed repeated hemarthrosis with chronic synovitis resulting in daily pain. In an effort to control his symptoms, he underwent radiosynovectomy with injection of Phosphorus-32 in the left ankle and right knee. He received 0.55 mCi of the radioisotope in the left ankle and 0.54 mCi in the right knee. Of note, entering the intra-articular space of the right knee was noted to be technically challenging due to joint space narrowing secondary to arthritic changes. The procedure was performed by an experienced pediatric orthopedic surgeon. Three attempts were required to enter the joint space, arthrogram was used to confirm needle placement, and joint fluid was aspirated prior to the injection of radionucleotide. Intra-articular steroids were used after the injection of P-32.

Five days following treatment, he presented with dull pain in the right lower neck and sternum that worsened with inspiration. There was no history to trauma to the chest. The patient denied weakness, tingling, swelling, or erythema. After 3 days of continued worsening symptoms, computed tomography (CT) angiogram was obtained and revealed right subclavian fatty stranding and nonspecific inflammatory changes involving the arteries in the right thoracic inlet (Fig. 1). Magnetic resonance imaging and angiography showed mural thickening and enhancement of the right subclavian artery, origin of the right common carotid artery, and right innominate artery with adjacent edema and without evidence of vessel narrowing or occlusion (Fig. 2). At this point a whole-body scan on gamma camera was considered but not completed as it was not expected to reveal beta emissions from the P-32. Nuclear medicine then performed a Geiger-Mueller (GM) survey with a pancake probe, which is quite sensitive for detection of beta particles. The survey demonstrated beta emissions in the left ankle, right knee, as well as elevated counts near the heart and a narrow elongated area along the sternum and extending toward the patient's right side. The GM survey meter detected 0.08 milliroentgens per hour (mR/hr) over the

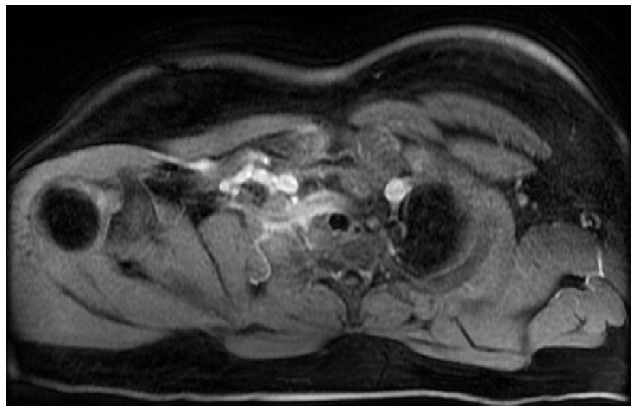

Fig. 2 – Delayed contrast enhanced MRI reveals mural thickening of the right subclavian artery, origin of the right common carotid artery, and right innominate artery.

right sternum and extending to the right upper chest. These findings indicate the possibility of P-32 inadvertently entering the circulation, during or after injection of the right knee despite confirmation of proper placement within the joint, travelling to the heart, and depositing in an area exposed to maximum cardiac output and increased blood flow, thereby leading to subclavian, carotid, and innominate arteritis with surrounding edema. The patient was treated with oral steroids and meloxicam, with complete resolution of his symptoms in 7 days. Vasculitis was entertained as a possible differential diagnosis, especially Takayasu's arteritis, as it is the most common in this age group and affects large blood vessels. However, there were no constitutional symptoms, arthralgias, or other organ involvement suggestive of Takayasu's arteritis. Furthermore, quick resolution of his symptoms argued against the diagnosis of chronic large vessel vasculitis. (Figs. 3–6)

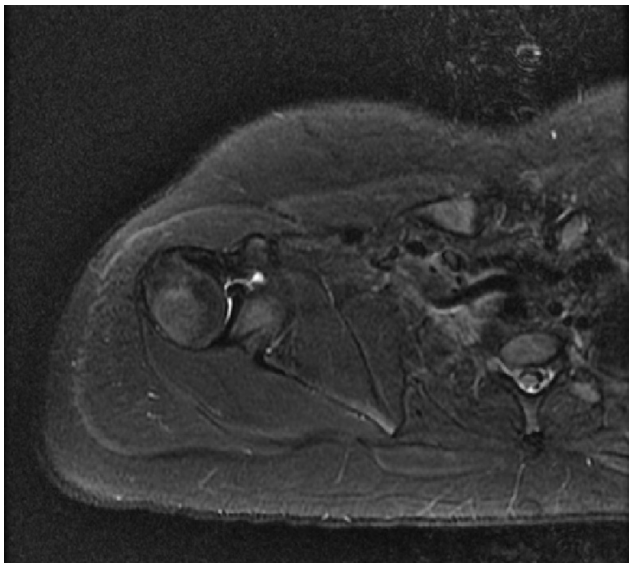

Fig. 3 – Axial STIR MRI image reveals perivascular inflammation of the right subclavian artery, with vessel wall thickening.

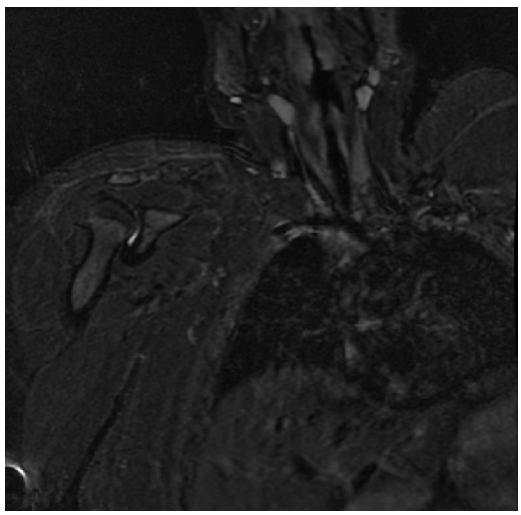

Fig. 4 – Coronal STIR MRI image reveals perivascular inflammation of the right subclavian and proximal right carotid artery, with vessel wall thickening.

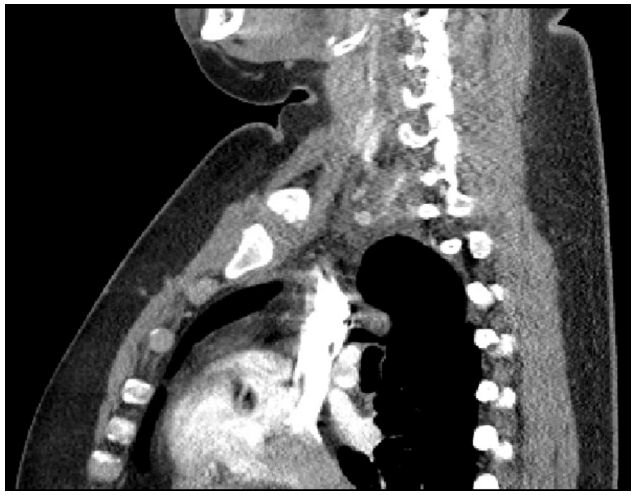

Fig. 5 – Sagittal reformatted CT angiogram reveals inflammatory changes of the right subclavian and proximal right vertebral artery.

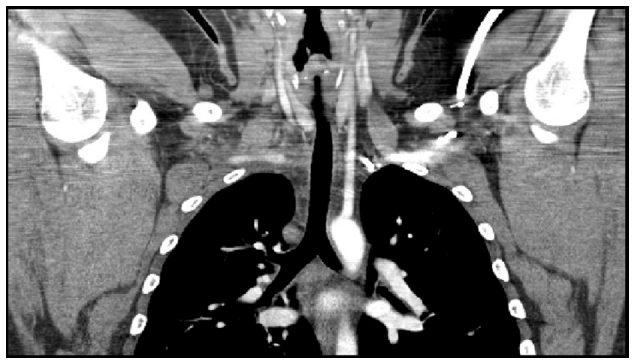

Fig. 6 – Coronal reformatted CT angiogram reveals inflammatory changes of the right subclavian with asymmetric soft tissue inflammation at the base of the right neck. Also, noted to have venous injection mixing in the left subclavian vessels.

Discussion

Although radiosynovectomy has been shown to be a minimally invasive and safe procedure with a low rate of complication, it nonetheless carries risk of potential hemorrhage, infection, and extravasation of the radioisotope from the joint space [4,5]. Two cases of pediatric acute lymphoblastic leukemia that developed within 1 year of undergoing P-32 radiosynovectomy have been reported in the literature [6]. P-32 colloid particles are in the range or 0.05-2 μm and are expected to end up in the reticuloendothelial system, mainly the liver, spleen, and bone marrow if inadvertently injected intravenously and along the right lower extremity upstream lymph node chains if leaked interstitially. There are reported cases of low-grade leakage from the intra-articular space into the lymphatic system, liver and spleen [7,8]. However, in most cases the incidence of extravasation is quite low and radioisotope is found to be present at low concentrations not thought to be harmful [3,8]. Other than the right subclavian, carotid, and innominate arteritis being an area of high cardiac output, it is unclear why leaked P-32 would deposit in that area. Localized involvement of the affected region cannot be completely explained by the high blood flow rate. However, the presence of vasculitis, adjacent edema, and positive emissions detected by the GM survey meter are supportive of radiation induced tissue damage in that area. To our knowledge, there have been no reported cases of arterial vasculitis caused by the radioisotope following radiosynovectomy. As the causation cannot be established, we can only claim it as possible complication.

Several isotopes of varying sizes and half-lives have been studied for use in radiosynovectomy. Phosphorus-32 is a pure beta emitter with a range less than 1 cm thereby reducing risk of radiation beyond the synovium [4,5,9]. Its large particle size decreases the risk of escaping the joint capsule, and its 14-day half-life allows P-32 to remain active in the joint for several days to slowly irradiate the surrounding tissue [4]. P-32 is delivered as a colloid suspension that includes dextrose, benzyl alcohol, sodium acetate, sodium hydroxide, and hydrochloric acid. It is certainly possible that one of these chemicals in the colloid, rather than the isotope itself, could have caused the vasculitic inflammatory changes. Nonetheless, the radioisotope was clearly detectable at the right thoracic inlet signifying systemic absorption and then deposition at the site of the right thoracic inlet. The arterial vasculitis seen in our patient represents a potential complication of radiosynovectomy that physicians should be aware of when considering this procedure.

Ethical approval

For this case report, formal consent is not required.

Institutional review board

This brief report describes a single case that does not meet the Department of Health and Human Services definition of "research", which is: "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge." Therefore, the activity has been deemed exempt from our institutional IRB approval.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2018.09.022.

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