

## Mesothelioma and venous thrombosis

Ami Schattner and Natasha Kozack describe and illustrate a unique and unfamiliar physical sign.<sup>1</sup> Better-known differential diagnoses for enlarged supraclavicular fossae include obesity and Cushing's syndrome. The one time that I observed such enlargement unilaterally was in an obese woman who had lost much supraclavicular soft-tissue volume through remote full radical mastectomy.<sup>2</sup> This patient's cortisol levels were normal.

With regard to Virchow's triad, the injury that predisposes to thrombosis damages the endothelium, not the epithelium, and the specific abnormality of blood flow is stasis. In the case described by Schattner and Kozack,<sup>1</sup> lack of flow was likely fostered not merely by proximity of the tumour but also by extrinsic compression of the internal jugular vein or any of the more proximal veins, such as the left innominate vein. The resultant venous stasis and venous hypertension would be transmitted to the internal jugular vein, which would in turn predispose to thrombosis of the latter. Alternatively, primary thrombosis that occurred proximally might have been propagated distally.

It would be of interest if Schattner and Kozack could report the state of the great veins at the time of surgery, on the basis of either imaging or direct observation during the operation, as well as the local findings if an autopsy was performed when the patient died, 3 months later.

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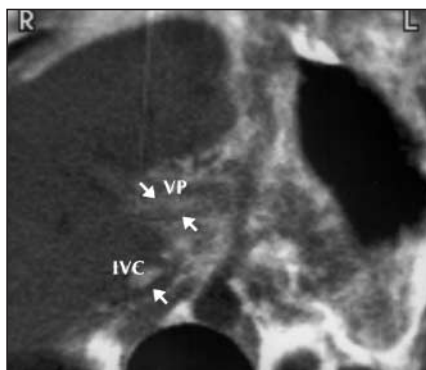
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Ami Schattner and Natasha Kozack report a case of mesothelioma in a man who exhibited jugular and subclavian vein thrombosis.<sup>1</sup> Malignant pleural mesothelioma is a relatively rare type of cancer that is reported to be associated with venous thromboembolism.<sup>2</sup> We describe here a patient with malignant pleural and peritoneal mesothelioma who experienced portal vein thrombosis. This patient had a history of exposure to zeolite, and ascites developed while the patient was being followed for the malignant pleural mesothelioma.

CT of the abdomen revealed diaphragmatic invasion of the right pleural mesothelioma. In addition to the peritoneum, the omentum and mesentery were diffusely invaded by the tumour. At the same level, the portal vein and the inferior vena cava both appeared to have a lucent lumen and exhibited contrast enhancement at the vessel wall (Fig. 1).

Cancer patients are prone to thromboembolic events, either as part of a paraneoplastic syndrome or because of a decrease in anticoagulation factors, such as prothrombin C, prothrombin S and antithrombin III, caused by some chemotherapeutic agents.<sup>3</sup> Mesothelioma cells and cell lines have been shown to secrete a pleiotropic cytokine,



**Fig. 1: Transverse CT scan demonstrates thrombosis (arrows) of both the portal vein (VP) and the inferior vena cava (IVC).**

interleukin 6, which potentiates the production of platelets.<sup>4</sup> In addition, mesothelioma cells release a sedimentable procoagulant material in vitro;<sup>5</sup> however, the underlying mechanism of thrombosis in mesothelioma is still a mystery.

Physicians who care for patients with mesothelioma should keep in mind that the thrombotic complication of the disease is not rare and may also involve a relatively unusual site, the portal system.

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### [One of the authors responds:]

We agree with Henry Schneiderman that in the patient we described<sup>1</sup> the proximity of the tumour to the thrombosed vessels was far from coincidental and that the tumour was likely material to the pathogenesis of thrombosis. One of 2 mechanisms could be involved: either, as Schneiderman suggests, mechanical compression of proximal veins causing venous stasis or elaboration by the tumour cells of spe-

cific procoagulants, whose concentration and effects are more prominent close to their site of origin. Both mechanisms have been demonstrated in patients with adenocarcinoma of the pancreas.<sup>2</sup> However, reports of thrombosis in patients with mesothelioma are much rarer than in patients with adenocarcinoma of the pancreas or lung, for example, which suggests that the first mechanism is the more likely in the case we described;<sup>1</sup> the chest CT shown in our report is consistent with this hypothesis. The surgery report did not allude to the state of the veins, and, unfortunately,<sup>3</sup> an autopsy was not authorized. As for our description of Virchow's triad, use of the word "epithelial" was a typographic error, and the text should have referred to "endothelial damage" (on page 465, third column).

The case reported by Mehlika Isildak and associates is an additional vivid reminder that cancer-associated thrombosis can affect veins at almost any site; it also emphasizes the greater risk with more advanced disease.<sup>1</sup> However, thrombotic complications in mesothelioma remain an unusual occurrence in both early<sup>4</sup> and advanced disease. Interleukin 6 (IL-6) may indeed be produced by mesothelioma and other tumours.<sup>5</sup> It affects not only the number of platelets but, more important, their function. Platelets responding to IL-6 have increased sensitivity to activation by thrombin and increased procoagulant activity, which may be further enhanced by the elevated levels of fibrinogen and plasminogen activator inhibitor (which suppresses fibrinolysis) caused by IL-6 and other inflammatory mediators.<sup>6</sup> The exact relevance of these observations to thromboembolism in vivo remains unproven.

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## Kickbacks and self-referral

Sujit Choudhry and associates<sup>1</sup> raise some excellent points in their discussion of the unethical nature of physician kickbacks and physician self-referral. An additional related behaviour is on the horizon for physicians in many provinces.

Electronic medical records and clinical management systems are now being promoted by federal and provincial authorities as a valuable component of care. One of the many functions currently being touted as desirable in a clinical management system is direct communication between the prescribing doctor and the patient's pharmacy for both new and repeat prescriptions.

For the vast majority of prescribing physicians and pharmacists, the ability to send a prescription to a pharmacy "at the touch of a button" will be a welcome relief from repetitive, illegible, hand-written prescriptions. For a few doctors and pharmacists, this function will represent an opportunity for hidden financial gain (through a kickback).

Time could be well spent asking questions about direct connections between a prescribing physician and a pharmacy. Provincial regulating authorities for both pharmacists and physicians should examine the risks and benefits of this functionality. They should also determine what reporting and control mechanisms are needed to

minimize the temptation of a destructive conflict of interest.

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Sujit Choudhry and colleagues<sup>1</sup> are to be congratulated for raising the troubling issues of physician kickbacks and self-referrals.<sup>1</sup> The Medical Reform Group, of which I am a member, agrees that these practices are ethically dubious and ought to be much more closely regulated.

One simple way to limit kickbacks and self-referrals would be to ban investor-owned independent health facilities from operating within the publicly funded health care system. Kickbacks and self-referrals exist chiefly to increase profit. Disallow profit, and these practices would probably wither away.

There is another reason to consider banning investor-owned independent health facilities: quality. In the United States at least, investor-owned hospitals<sup>2</sup> and dialysis centres<sup>3</sup> are associated with higher mortality rates than private, nonprofit facilities. Similarly, in a study comparing for-profit and nonprofit health maintenance organizations in the United States, the nonprofit organizations outperformed the for-profit ones on all of the 14 quality-of-care indicators that were assessed.<sup>4</sup> In the Canadian context, for-profit independent health facilities are most common in the diagnostic services (e.g., laboratory testing and imaging) and rehabilitation (e.g., physiotherapy) sectors. Given the US data (there are none from Canada), there is no reason to assume that the services they provide are as good as those provided by nonprofit operators.